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Pictured at the Smithsonian Institution, Washington, D. C., during the judging of entries submitted for the First International Salon, "Photography in Science," are (*left to right*): A. Aubrey Bodine, associate editor, *Camera Magazine;* K. M. Endicott, Division of Pathology, U. S. Public Health Service; Ralph D. Bennett, technical director, Naval Ordnance Laboratory; Alexander Wetmore, secretary, Smithsonian Institution; F. L. Campbell, editor, *The Scientific Monthly*; and A. J. Wedderburn, Division of Graphic Arts, U. S. National Museum. (See *News and Notes.*)

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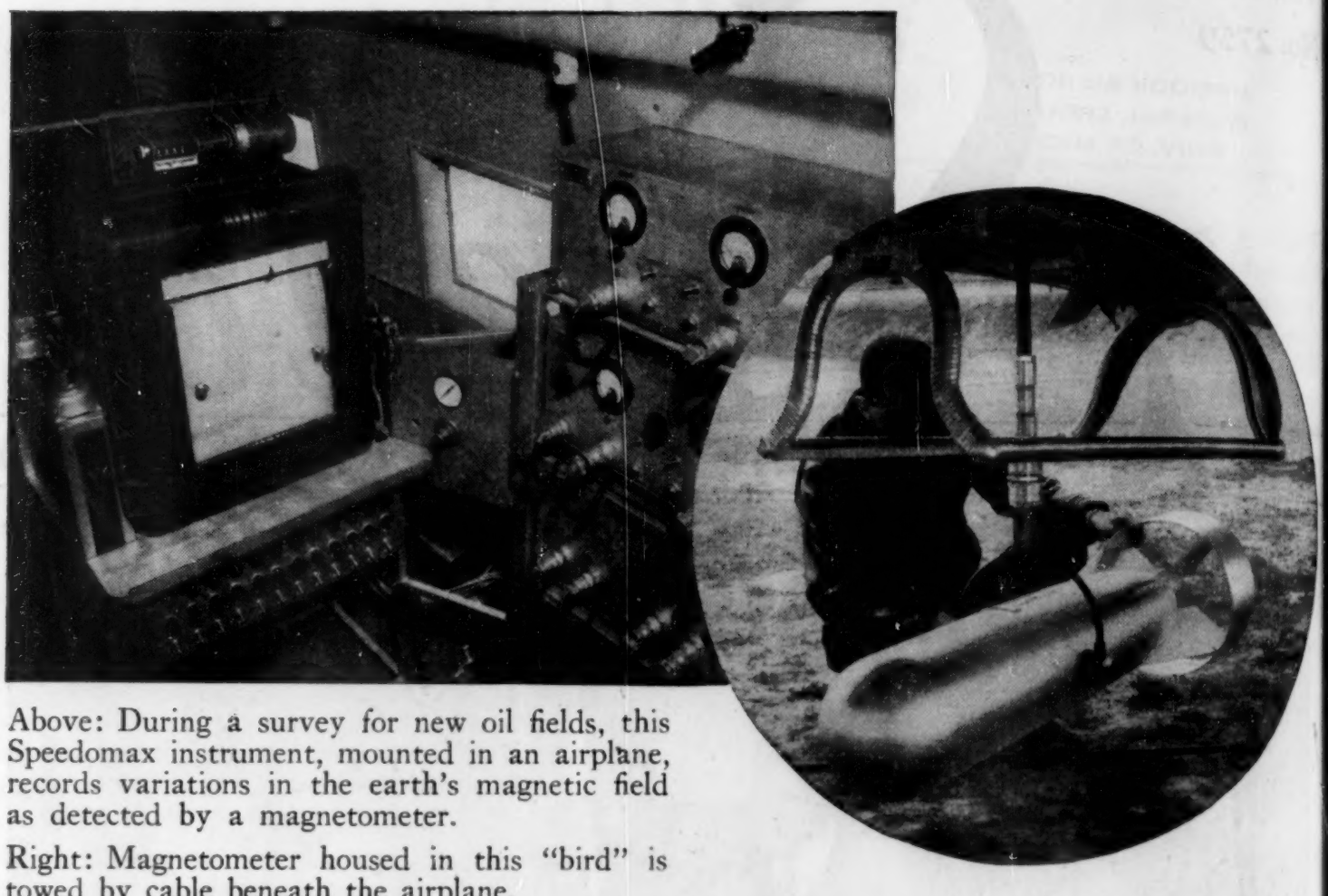
Biology of Cancer

A. C. Ivy



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Right: Magnetometer housed in this "bird" is towed by cable beneath the airplane.

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Biology of Cancer

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I BELIEVE THAT CANCER IS THE MOST challenging disease which confronts biological science. It involves the most basic phenomenon in biology, namely, growth. It is characterized by an abnormal, unlimited, unregulated growth of tissue which destroys the host which nourishes it. It is unique among diseases because the host is consumed by its own flesh. The thought of this fact, the frequently associated pain, and the insidiousness and treachery of its attack place cancer first among the most dreaded diseases.

The basic principles of cancer as a descriptive science were known to Galen (150 A.D.), who recognized three classes of tumors. The tumors of his third class were referred to as "tumors contrary to nature." They were called "contrary to nature" because of their abnormal and unregulated growth and frequently destructive character. There were two types, one benign and the other malignant; the latter was called "cancer."

About the middle of the 19th Century, when it became generally agreed that a cancer consisted of cells, two hypotheses regarding the nature of cancer received recognition. One maintained that normal cells can be transformed into cancer cells by irritation or infection of some type; the other, that the cells which form cancer were cancerous from embryonal life as the result of an hereditary blemish or an embryonal rest of cells excluded from the line of normal development.

These are the principal ideas contributed by the descriptive scientific approach to the problem of the cause of cancer. In addition much important and very valuable information which led to the morphologic classification and diagnosis of the disease was accumulated.

The descriptive science of cancer added nothing to the treatment of the disease, since therapeutics is entirely an experimental science. And, it is generally agreed that the cause of a disease remains a theory until established by controlled experimentation.

The study of cancer as an experimental science began just prior to the turn of the century, when cancer was first transplanted in laboratory animals by Hanau (1889) and Moreau (1891)—a fact which was soon confirmed by Leo Loeb (1901) and Jensen (1902). Since then, spontaneous cancer has been observed in almost all species of animals; cancer susceptibility has been bred into and out of animals; cancer has been produced by various types of chemical substances (carcinogens); and the chemotherapeutic action of hundreds of chemical compounds have been assayed on animals with transplanted tumors. This approach has contributed a mass of basic information to the problem of cancer. Moreover, all the knowledge, tools, and techniques of biology and medicine and of chemistry and physics have been focused on the problem. No known aspect has escaped some experimental attention. Many facts have been established, and a few optimistic experienced students of the problem believe that so much has been discovered in the last 20 years that the therapeutic control of advanced cancer is "just around the corner."

One of the most significant contributions of the last 25 years has been *the unequivocal proof* that cancer can be cured by removal or destruction if recognized early enough. But the grim and urgent problem is to prevent, cure, or control advanced cancer.

The most productive research for the treatment of advanced cancer, from the viewpoint of present applications, has been the development of the hormonal relationships to cancer of the prostate (*10*) and breast (*9*). This success clearly demonstrates that the most significant work to be done in the forseeable future is basic research, both experimental and descriptive. The currently sick must be cared for, of course; but we must look also toward the future saving of millions of lives.

The advances in the basic knowledge of cancer have not yet answered with certainty some of the fundamental biological questions.

What is the difference between a benign and a malignant tumor?

At present it is not possible to draw a clear line of distinction between a benign and a malignant tumor except to say that, when a benign tumor starts to invade and metastasize, it has undergone malignant transformation. That such may occur has been demonstrated experimentally, e.g. the Shope papilloma (*24*), and the papilloma induced with tar (*11*), and the clinical evidence is strongly presumptive (*27*).

Invasiveness and metastasis do not always signify that a tumor is a cancer or truly destructive of the host. For example, the chorionic villi (fetal part of the placenta) invade the endometrium (uterus) up to a stage of placental development and then act like a benign growth, even though the placental tissue has a carbohydrate metabolic pattern like malignant tissue (*7*). Also, during pregnancy chorionic cells enter the blood stream and lodge in the lungs, but they do not form tumors there. The chorioadenoma extensively invades the wall of the uterus and surrounding structures and may even metastasize to

This address was presented at the Fourth International Cancer Research Congress, St. Louis, Missouri, September 3, 1947.

the lungs, but tumors are not formed or, if so, they regress. The choriocarcinoma, however, invades, metastasizes, and destroys the host (*5*).

Some believe that a benign colloid goiter (tumor of the thyroid gland) may metastasize to the lungs of man and dogs (*5*). According to my own experience obtained between 1918 and 1925, when all the adult dogs in Chicago were goiterous, I found evidence of local invasiveness in some 10 dogs in which thyroid metastases were formed in the lungs. I was unable, however, to produce lung tumors by introducing small pieces or a "cell" suspension of a thyroid which appeared to be "carcinomatous" into the external jugular vein. This may have been due to the heterologous nature of the tissue used or to other factors. Dr. Huggins, of the University of Chicago, has informed me that he has been unsuccessful when he similarly used hyperplastic prostatic tissue in the dog.

Between 1918 and 1925 I autopsied approximately 2,000 adult dogs in Chicago among which the incidence of goiter was 98 per cent and of "cancer" of the thyroid with gross pulmonary metastases, 1.6 per cent. Goiters and cancer of the thyroid completely disappeared from Chicago dogs after 1925, or one or two years after iodized salt became a general grocery store commodity.

It is difficult, for these and other reasons, to avoid the view that, fundamentally, benign and malignant tumors are manifestations of the same neoplastic principle, the benign tumor or cell representing an arrested or inhibited stage of a potentially malignant process.

Does the cancer cell represent a transformation of a normal cell or a cell abnormal from embryonic life?

All the evidence with which I am familiar may be interpreted as indicating that the cells transformed into malignant cells may arise either from embryonal residues or from normal cells which are more susceptible than other normal cells in the same organ. Even the apparent transformation of fibroblasts into sarcoma cells in tissue culture by treatment with methylcholanthrene, as observed by Earle (*21*), is not sufficiently free from a possible experimental error to invalidate the theory of embryonal residues being involved.

But it is really immaterial, except from a taxonomical point of view, whether a normal cell or an "embryonical residue" is changed. This is true because the growth of fetal tissues and the placenta throughout their normal course is regulated, regardless of the fact that they have a metabolic pattern like malignant tissue. The important biological question is:

What is the nature of the process induced either into the normal cells or, if one prefers, the "embryonal residue" when they become cancerous or truly malignant?

The nature of "the autonomous" or "the malignant process" still appears to be the most fundamental question pertaining to the biology of cancer. It would appear that the rational approach to the secret of the cure of cancer is to ascertain either the factors which are responsible for causing unregulated, unlimited, invasive, metastatic, and destructive growth or those which are responsible for limiting and regulating normal growth.

The autonomous nature of cancer. A tumor is sometimes defined as "an autonomous new growth of tissue" (Ewing). Autonomous implies growth unregulated and independent of the host except for nourishment. Malignant implies destructiveness due to invasiveness and metastasis.

If a malignant growth is entirely autonomous except for nourishment, nothing manufactured in the body of the host except food of some type could influence it. This is not true of some cases of cancer of the prostate with metastasis to the bone in man, since Huggins and his colleagues and others (*10*) have observed the disappearance of metastases in bone and the primary tumor after castration or the administration of large doses of stilbesterol to the patient. The cells of tumors of the prostate and breast which are markedly benefited by modifying the sex hormone supply may not be sufficiently transformed to be entirely autonomous. Of course, it may be that in the case of the prostate, one is dealing with a very special case, since its embryonal development is specifically stimulated or inhibited by male and female sex hormones, respectively. In this connection it would be of interest to know what effect testosterone might have on chorioadenoma (v.s.) and choriocarcinoma (v.s.). It would also be significant to know the effect of the growth-promoting activities of the thyroid gland (*19*) and the anterior lobe of the pituitary gland on the growth of cancer. Would the so-called "anti-hormone" of the thyrotropic hormone produced by the hypophysis affect a carcinomatous thyroid?

The autonomous nature of a malignant tumor should not be viewed too rigidly. A rigid adherence to this hypothesis is probably contrary to the facts, and its pessimistic implications tend to retard discovery of knowledge regarding the nature and cure of cancer. In fact, when one considers all the factors inside and outside the cell which affect growth and the great care which must be exercised in the tissue culture of malignant cells, it is difficult to accept the view that any tumor is completely autonomous relative to its rate of growth, even though it may be completely autonomous in regard to its invasive and metastatic properties.

The uniformity of the chemistry of malignant tissue. The strongest evidence that the malignant process is identical, in what may be termed fully transformed malignant tissue, has been obtained primarily from naturally occurring and artifically induced transplantable tumors. It shows that a marked similarity exists in the chemical properties (composition, enzyme, and metabolic pattern) of a malignant tissue regardless of the species or the histogenetic source of the tumor tissue (*7*). Malignant tissues as a class appear to be as unique chemically as liver tissue or gastric mucosa. I have been particularly awed by the chemical and metabolic similarity of the tissue of a hepa-

oma (metastasizing tumor of a rat's liver) and a gastric denocarcinoma (cancer produced artificially in a rat's tomach), two tissues which in normal life appear to have very little in common. I have also been impressed by the act that very rapidly regenerating hepatic tissue has a ormal metabolic pattern, whereas hepatoma tissue has he metabolic pattern of malignant and fetal tissue (*7*). The chemical results, of course, support the old theory hat malignant tissue represents a reversion to an embryonic type of cell, the growth and reproduction of which is exquisitely regulated and limited. This apparent uniformity of the chemical pattern of malignant tissue may represent an oversimplification, as has been suggested by biochemists working in this field. Regardless of their remarkable contributions, these biochemists recognize that their chemical techniques are still relatively crude and that our knowledge of the chemistry of the normal as well as the cancer cell is in a pioneer state.

If the chemistry of malignant tissues or the malignant process is identical for all malignant tumors and if it is significantly different from normal tissue, one therapy should be applicable to all malignant tumors. The alternate assumption is that the various cancers represent separate malignant processes, or different stages of the malignant process, and a therapy for each will have to be discovered. Morphologically the organ of origin of a malignancy is recognizable in approximately 90 per cent of the cases seen clinically in man. This would suggest that there may exist some competition or overlap between the chemical pattern of the original normal cell and the malignant cell. With present methods this possibility cannot be analyzed with certainty because such a tumor may contain a variable number of premalignant and malignant cells. The answer to this question probably awaits the development of histochemical methods which would reveal the difference between the chemistry of a normal adult cell, an irritated adult cell, a precancerous cell, and a malignant cell. There is no evidence which would show that a cell today has the metabolic pattern of a normal cell and, at the next division, that of a malignant cell. There are geneticists (*25*) who believe that such a somatic mutation may occur and point out that it may explain the alleged "irrevocable character of the malignant change." If such does occur, the fundamental chemical nature of the malignant process could still be the same and respond to a uniform therapy.

Although the malignant process may be essentially the same in all malignant tissues, it may be conditioned or controlled by several factors which vary with the etiology and the tissue from which the tumor arises. If the therapeutic evidence we now have has any bearing on the nature of the malignant process and the factors which condition it, each type of tumor may demand a separate therapy. For example, hormones are used successfully in the treatment of cancer of the prostate and breast; the X-ray sensitivity of various tumors varies widely; and, a definite difference exists in the ease with which toxic substances cause hemorrhage in an experimentally induced sarcoma and carcinoma.

In my thinking of cancer, I frequently use analogously the animal parasites. The "heart worm," or the adult canine filaria, receives its nourishment from the host; it is autonomous with respect to its own growth and reproduction; it is a unique tissue and has a unique metabolism which, however, is probably different from that of other parasites as well as tumor tissue, because its cells are differentiated. Is our problem in cancer, as in the case of parasites, to find a substance which is toxic or essential for each type of cancer, or is it to find one which will be toxic or essential for all cancers? In view of our ignorance, we shall have to accept both as working hypotheses.

In view of the fact that the change in the chemistry and metabolic pattern of a normal or "irritated" tissue into that of malignant tissue is relatively abrupt and distinct in some known respects (*7*), I firmly believe that ways will be found for systemically destroying malignant cells without destroying the normal cells of the host. This is apparently what the X-rays or gamma rays do in the case of cancer of the skin (*6*). I remember being told as a student that gallstones could never be dissolved without dissolving the tissues of the host. Yet, thanks to skeptics who experiment, we now know that if gallstones are placed in the gall bladder of a dog, they are dissolved quite rapidly; so the problem of the solution of gallstones is to find a way to change the fatty acid-cholesterol ratio in human bile toward that found in dog's bile. Similarly, the chemical data obtained on cancer provide much hope and encouragement for the view that further studies will answer the crucial question of the nature of the malignant process, or at least show the way to the proper systemic therapeusis.

Multiplicity of causative factors in tumor genesis. One of the best examples of the multiplicity of factors concerned in the induction of tumors comes from the intriguing studies of the natural occurrence of mammary cancer in many inbred strains of mice. At least three factors are involved: (1) a genetic constitution, or pattern, or inherited susceptibility; (2) the female sex hormone; and (3) the "virus-like" agent transmitted in the milk of the mice (*3*). For example, estrogen must be given to male mice before they will develop the tumor, and spayed females will not develop the tumor unless given estrogen. Though the inciting agent is present in all of the tissues of the exposed mouse, it predisposes only to mammary tumors. In addition, the age at which the agent is introduced is a factor. Even with the best-known combination of these factors, some 9 months are required for the appearance of the tumor, or the latent period of induction is very long in the life of a mouse. And further, though rabbits and rats form a neutralizing antibody for the milk factor, the mouse does not, and an antimouse tissue serum has no effect on it. Finally, though other factors probably exist, the diet

during the period of tumor development exerts an influence on the incidence of the mammary tumors in mice (*26*).

Many other examples exist showing the complexity of the endogenous and exogenous factors concerned in the genesis of cancer in mice. To render the problem still more complex, the species differences are marked, and the influence of factors which predispose to cancer in one species may retard in another species. For example, though reproduction and nursing unequivocally predispose to cancer of the breast in the strains of female mice studied, it has the opposite effect on women.

Paucity of information on the dietary control of cancer. When one reads the literature on the successful inhibition of tumor induction and growth by dietary control, one becomes acutely aware of the paucity of information in this field in relation to its demonstrated importance. Very little is known regarding the existence of any specific nutritional requirements of any kind of tumor, except the hepatoma in the rat, where diet exerts a very significant effect. In view of the fact that specific dietary factors are required for the maintenance, reproduction, and growth of normal cells and that the metabolic pattern of malignant tissue is quite specific and may be found to be more so, it would seem to be advisable to cultivate this field intensively in man as well as animals.

The natural resistance or immunity of certain tissues. One of the most provocative phenomena in the field of cancer is the natural resistance of certain tissues to the natural development of cancer and the acceptance of metastases. Striated muscle, heart muscle, spleen, kidney, and intestinal mucosa are particularly resistant to the development of malignant tumors. In lower forms this applies also to the mucosa of the glandular portion of the stomach. The natural resistance of these tissues has rendered it very difficult for the geneticist to render them susceptible. Yet, we know that tumors of all these organs do occasionally occur, and particularly so in the stomach and large intestine of man. We have no rational notion for the explanation of this natural resistance even in the presence of high-grade susceptibility in other organs. It is not due to a natural resistance to the transplantation of an homologous tissue because thyroid, bone, and other tissues have been transplanted into the spleen and striated muscle.

It is possible to render an animal immune to grafts from another animal (heterologous grafts) depending on the natural resistance of the host and the malignancy of the tissue to be transplanted. This is particularly true when a graft has regressed or, after "taking," has been destroyed by X-ray treatment. But up to the present time no one has demonstrated antibodies to cancer tissue in the serum of the host or has been able to demonstrate in a host immunity to a graft of its own cancer (*1*, *17*).

However, immune reactions have been obtained from the serum of a host with a heterologous transplant and have been explained as due to heterologous tissue proteins (*17*). (It would seem that in such a case the proliferative power of the transplant must be such as to annul any injurious effect of the antibodies, if they have an injurious effect.) The failure to obtain evidence of antibodies in the serum of animals with malignant tumors is consonant with the chemical similarity of proteins in malignant tissue and the normal tissue from which it came (*7*). Antigenically, a crystalline enzyme isolated from the Jensen rat sarcoma was the same as that from rat muscle (*16*). On the contrary, it has been reported that a cathepsin containing protein isolated from a hepatoma (rat) is antigenically more similar to one isolated from a Jensen sarcoma (rat) than that isolated from the normal liver (*18*).

It is discouraging to read the literature dealing with the immunology and serological diagnosis of cancer. Ehrlich (*4*), who worked with the problem for 15 years, is said to have become so discouraged that he stated: "Until some fundamental discovery has solved the mystery of life itself, our knowledge of cancer will not advance a single step." Although an attempt such as Ehrlich made to immunize the body against cancer by inducing resistance against transplantable cancers may not be achieved, work using the new methods for isolating protein and the newer knowledge and techniques of immunochemistry should be applied. At the same time the possibility of developing a method for the serodiagnosis of early cancer should not be overlooked, even though it may be grossly empirical.

The need of a simple test for the diagnosis of early internal cancer is urgent. Cancer of the alimentary tract ranks first as a cause of death from cancer. Cancer of the stomach ranks first in men and second in women. Cancer of the stomach is "silent" or produces no symptoms in 25–30 per cent of autopsied persons dying of the disease (*14*). In fact, the evidence indicates that the disease is overlooked in 50 per cent of the cases which are attended at our best general hospitals, for the incidence of gastric cancer, according to mortality statistics, is 16 per cent of all cancers, and the incidence, according to the records of general hospitals is only from 6 to 8 per cent of all cancers. (Any challenge of these data, which I admit may be in error, simply indicates that we need to increase the descriptive science of the disease.) Not only does a large percentage of silent cases exist, but at least 20 per cent of people die of a surgically resectable cancer or without metastases beyond the adjacent lymph nodes (*22*). The surgical mortality from gastric resection has been reduced to such an extent that it is now possible to state that if we had some simple method for the diagnosis of early gastric cancer, the mortality from this disease could be reduced by from 30 to 50 per cent, and perhaps even more.

The effect of cancer on the host. If early cancer cannot be diagnosed by some serological method, some effect of the cancer on the host may be found before metastasis occurs or after it has occurred to the immediately adjacent lymph nodes, as in the case of the phosphatase test for cancer of the prostate. In fact, the success of this test pro-

vides renewed hope that a test or tests for other internal cancers may be found.

The most striking early effect of a cancer on the biochemistry of the host that seems to be established is the reduction of renal and hepatic catalase. The catalase in the erythrocyte is unaffected. This appears to be specific for a malignant tissue, since it is common to malignant tumors and since the phenomenon does not occur in pregnancy or in the presence of embryonal transplants. According to Greenstein and Andervont (*8*), the liver catalase is significantly reduced in four days after transplantation of a sarcoma in the tail of a mouse. Whether the reduction in renal and liver catalase is unique for a malignant process and what causes it is uncertain.

I select this example of the effect of a malignant tumor on its host only to emphasize that such an approach to the diagnosis of cancer is feasible and, if successful, should contribute greatly toward facilitating the case-finding of internal cancer. There are other leads with promise. In fact, it is improbable that a single diagnostic method for all types of cancer will be found. Several methods may have to be used in a case-finding program.

TABLE 1

SHOWING THAT PRIMARY CARCINOMA OF THE LIVER IS EQUALLY DISTRIBUTED BETWEEN WHITES AND NEGROES AT COOK COUNTY HOSPITAL, CHICAGO, WHERE ONE-THIRD OF THE AUTOPSIES ARE ON NEGROES*

	White	Colored	Total	Per cent of total
Cancer with cirrhosis	22†	10‡	32	44
Cancer without cirrhosis	26§	14§	40	56
Totals	48	24	75	

* Data supplied by Dr. Hans Popper.
† All males.
‡ Three females.
§ Males predominate.

We should remember that the matter of diagnosis will still exist after a cure is found and that we now have the cure for many early cancers.

Man is at present an experimental subject for the study of cancer, as various investigators have pointed out. He is inclined to experiment on himself and produce disease that he might otherwise avoid. Hence, reliably collected and analyzed statistics should provide valuable information regarding the cause and prevention of cancer—particularly cancer of the stomach. For example, present statistics indicate that cancer of the stomach occurs twice as frequently in the Dutch as in the British. Is this true? And, if so, what is the cause? It has been ascribed to the greater consumption of irritants in the food and drink by the Dutch. The evidence is equivocal (*12*). The same situation obtains for the Chinese in Java who have a higher incidence of cancer than the native Javanese who have a low incidence (*12*). Statistics from England indicate that the incidence of cancer of the stomach is higher in the lower- than the higher-income group (Stevenson, 1921). Taking another internal cancer, the autopsy incidence of primary cancer of the liver in the South African Bantu is 37.5 per cent (*15*). In the West African Negro the disease represents 18.7 per cent of all deaths from cancer. In European countries cancer of the liver makes up only 1.1 per cent of all cancer deaths. Statistics from the Cook County Hospital, Chicago, show that this marked difference in the incidence of primary cancer of the liver between whites and Negroes can hardly be due to a genetic difference. At autopsy primary cancer of the liver constitutes 1.1 per cent of all cases of cancer as in Europeans, and the incidence is the same in the whites and Negroes (see Table 1). Such observations strongly indicate that extrinsic factors are concerned in the genesis of cancer of the stomach and liver. This should warrant and stimulate a thorough search among foods and drinks for carcinogenic agents. An agent in heated fats and something produced by heating cholesterol have been shown to cause sarcoma occasionally when injected subcutaneously in mice or rats. Nevertheless, it has not been established that the feeding of heated fat, cholesterol, or irradiated cholesterol will cause cancer of the stomach in the experimental animal. However, P. R. Peacock (*23*) observed a cancer of the stomach to develop in one of 6 rats when some croton oil was added to heated (350°C.) cotton-seed oil. The fact that one can demonstrate carcinogenic substance in heated fats (to the point of browning) by subcutaneous injection should render them suspect when taken daily over years. We should recall that in the case of gastric cancer in man we are looking for the cause of a disease which occurs only in approximately 1 out of 750 persons above the age of 40 (*13*). Also, a long latent period can be anticipated because a feeble carcinogen must act over a long period to induce a tumor—perhaps 30 years or more in man. The story of the experimental demonstration of the carcinogenic activity of tar should suffice to illustrate this point. Tar is a feeble carcinogen compared to the benzpyrene which was extracted from it.

I have taken advantage of this occasion to give special mention to the problem of gastric cancer because it heads the list of the organ sites for cancer in man. We know less about its cause and diagnosis than any of the external cancers. Gastric cancer has been neglected by the investigators in the field of cancer probably because it has not been easy to produce by genetic procedures and exogenous carcinogens.

In view of the progress in the basic knowledge of cancer made during the last 20 years and the availability of new chemical and physical tools, and the fact that funds appear to be forthcoming for an attack on all fronts, the possibility of great discoveries being made in the next 10 or 20 years looks very encouraging.

References

1. ANDERVONT, H. B. *U. S. Publ. Hlth Rpts*, 1932, 47, 1859.
2. BECK, S., KIRBY, A. M., and PEACOCK, P. R. *Cancer Res.*, 1945, 5, 135; BECK, S., and PEACOCK, P. R. *Brit. med. J.*, 1941, 2, 81.

3. Bittner, J. J. *Research Conferences on Cancer*, AAAS, Washington, D. C., 1945.
4. Ehrlich, P. *In* Oberling, C. *The riddle of cancer*. (Trans. by W. H. Woglom.) New Haven: Yale Univ. Press, 1944; *Z. Krebsforsch.*, 1907, 5, 59.
5. Ewing, J. *Neoplastic diseases*. (4th ed.) Philadelphia: W. B. Saunders, 1940.
6. Failla, G. *Amer. J. roent. rad. Therap.*, 1940, 44, 649.
7. Greenstein, J. P. *The biochemistry of cancer*. New York: Academic Press, 1947.
8. Greenstein, J. P., and Andervont, H. B. *J. nat. Cancer Inst.*, 1942, 2, 345.
9. Haddow, A., Watkinson, J. M., and Paterson, E. *Brit. med. J.*, 1944, 2, 393.
10. Huggins, C. *J. Amer. med. Ass.*, 1946, 131, 576.
11. Iball, J. *Amer. J. Cancer*, 1939, 35, 188.
12. Ivy, A. C. *J. nat. Cancer Inst.*, 1945, 5, 313.
13. Ivy, A. C. *J. nat. Cancer Inst.*, 1947, 7, 404.
14. Kark, R. M. *Gastroenterology*, in press.
15. Kennaway, E. L. *Cancer Res.*, 1944, 4, 571.
16. Kubowitz, F., and Ott, P. *Biochem. Z.*, 1943, 94, 314.
17. MacKenzie, I., and Kidd, J. G. *J. exp. Med.*, 1945, 82, 41.
18. Maver, M. E., and Barrett, M. K. *J. nat. Cancer Inst.*, 1943, 4, [illegible]
19. Morris, H. P., Dubnik, C. S., and Dalton, A. J. *J. nat. Cancer Inst.* 1947, 7, 159.
20. Nathanson, I. T. *New Engl. J. Med.*, 1944, 231, 764, 795.
21. Nettleship, A., and Earle, W. R. *J. nat. Cancer Inst.*, 1943, 4, 2[illegible]
22. Pack, G. T., and Livingston, E. M. *End results in the treatment of gastric cancer*. New York: P. B. Hoeber, 1939.
23. Peacock, P. R. *J. nat. Cancer Inst.*, 1947, 7, 407.
24. Rous, P., and Friedenwald, W. F. *J. exp. Med.*, 1944, 79, 511.
25. Strong, L. C. *J. nat. Cancer Inst.*, 1945, 5, 339.
26. Tannenbaum, A. *Cancer Res.*, 1942, 2, 460; Husby, R. A., Ball, [illegible] B., and Visscher, M. B. *Cancer Res.*, 1945, 5, 40; White, F. R. *J. nat. Cancer Inst.*, 1944, 5, 41.
27. Wangensteen, O. H. *J. Amer. med. Ass.*, 1947, 134, 1161.

Recent Changes in Sedimentation in the Gulf of Mexico

Parker D. Trask, Fred B. Phleger, Jr., and Henry C. Stetson[1]

THAT SEDIMENTS IN THE GULF OF Mexico have changed materially in relatively recent time has been established by a recent expedition of the *Atlantis*, the oceanographic research vessel of the Woods Hole Oceanographic Institution. Deposits clearly associated with the Ice Age lie within a foot or two of the surface of the sea floor over a large part of the Gulf.

The *Atlantis* spent the months of February and March 1947 in the northwest part of the Gulf of Mexico, primarily for the purpose of investigating the environmental conditions of deposition of sediments. The expedition was sponsored jointly by the Woods Hole Oceanographic Institution and the Geological Society of America. The latter contributed a grant of $14,500 for this purpose to the authors of this communication, while the Oceanographic Institution supplied the vessel, crew, and scientific personnel for the expedition and made available laboratory facilities and personnel for working up the results.

Despite considerable rough weather, the expedition was remarkably successful. Some 550 short cores of the bottom sediments, ranging in length from 5 to 50 cm., and 100 long cores, ranging in length from 1.5 to 3.3 m., were collected. Twelve lines of samples transverse to the coast across the continental platform from the mouth of the Rio Grande to the mouth of the Atchafalaya River, and 7 lines across the continental slope out to the deepest part of the Gulf, were taken. In addition, about 100 stations were occupied for plankton tows, serial temperature, and samples of water. Several hundred temperature-depth records were made with a bathythermograph along the lines of traverse, and continuous depth records were made with a recording fathometer. The material collected is now being actively worked up at the Woods Hole Oceanographic Institution. The U. S. Bureau of Mines Experimental Station at Pittsburgh, Pennsylvania, through the courtesy of H. M. Cooper, supervising chemist of the Coal Analysis Section, is cooperating in this work by making analyses of the organic content of the sediments.

A preliminary examination of 12 long cores distributed representatively throughout the off-shore waters of the Gulf shows two distinctly different layers of sediment: (1) an upper zone of globigerina ooze, rich in calcium carbonate, 5–50 cm. in thickness, and (2) a lower zone of alternating bands of clay and extremely well-sorted, fine-grained silt, relatively poor in calcium carbonate. Although in a few places the two zones are separated by a layer of red clay or red mud of intermediate calcium carbonate content, in most cores the transition from alternating clay and silt to globigerina ooze is fairly abrupt. Cores from the area off the Rio Grande contain a few centimeters of foraminiferal ooze at the top, below which is fine silt extending to the bottom of the core. No alternating bands of clay and well-sorted silt have been noted in this area.

The lower zone of banded clay found throughout most of the Gulf consists of alternating layers of clay, 1 mm. to 30 cm. thick, and of silt, 0.2 mm. to 5 cm. in thickness. Most of the clay bands are 1–2 cm. thick; most of the silt bands, less than 1 mm. The silt is so well sorted that under a high-power binocular microscope it has the appearance of ordinary beach sand. Its average (median) diameter is estimated to range between 10 and 20 μ. Such good sorting in such a fine silt is most unusual.

Well-defined cross-bedding was noted in two cores: one, at a depth of 170 cm. beneath the sea floor in a sample taken from a sea mount near the edge of the con-

[1] The authors are associated with the U. S. Geological Survey, Washington, D. C., Amherst College, Amherst, Massachusetts, and the Museum of Comparative Zoology, Cambridge, Massachusetts, respectively.

This paper has been published with the permission of the director, U. S. Geological Survey.

tinental platform, and the other, 50 cm. beneath the sea floor in the abyssal deep near the edge of the continental slope off Campeche bank, north of the Yucatan peninsula. In the sample from the deep off Campeche bank, the false-bedded zone is 5 cm. thick, individual layers dipping up to 15°. The core there was not deformed, and the attitude of the bedding must be regarded as genuine.

One core (No. 143), taken in 3,546 m. of water in the middle of the Sigsbee deep in the deepest part of the Gulf, has been examined for Foraminifera. The upper foraminiferal zone, 50 cm. in thickness, is characterized by a subtropical planktonic fauna, dominated by *Globigerinoides rubra*, *Globorotalia menardii*, *G. tumida*, *G. truncatulinoides*, and *Pulleniatina obliquilata*. Between depths of 50 and 68 cm., in a zone of red clay or red mud, the fauna is transitional between cold- and warm-water forms. Between depths of 74 and 78.5 cm., at the top of the zone of banded clay and silt, the fauna is definitely sub-Arctic and is dominated by *Globigerina bulloides*, *G. pachyderma*, and small specimens of *Globigerinoides rubra*. Between 78.5 and 125 cm., the fauna is cold-water in type but is warmer than that between 74 and 78.5 cm.; and from 125 to 168 cm., at the bottom of the core, the fauna is definitely sub-Arctic. Abundant broken and seemingly eroded specimens were noted between 74 and 78.5 cm., 92 and 96 cm., and 113.5 and 116.5 cm.

A series of submerged hills rise above the sea floor near the outer edge of the continental platform, just inside the 100-fathom line, off the Louisiana coast between the Sabine and Atchafalaya Rivers. Two of these hills, lying within 10 fathoms of the surface, located in N. Lat. 27° 52.5′, W. Long. 93° 49′, and N. Lat. 27° 54.5′, W. Long. 93° 36′, were studied in some detail. The fathometer trace shows that they are remarkably flat on top and that they rise rather abruptly 300–400 feet above the surrounding muddy plain. On the side of one of these two hills the depth changed from 51 to 86 fathoms within a few ship lengths.

The sediments in these areas are influenced materially by the change in topography. The flat continental platform is underlain by sandy silt; the slopes of the hills, by silty, calcareous sand; and the tops, by round Lithothamnium balls and little or no sandy material. The Lithothamnium balls, dredged from water up to 20 fathoms in depth, have a maximum diameter of 10 cm. and seem to be alive on all sides, which suggests that they are rolled around by the waves or currents. In one place in 9 fathoms of water, several genera of corals, similar to common West Indian genera, were found with these balls.

The origin of these hills arouses speculation. Shepard (*2*) has suggested that they are salt domes. Trowbridge (*3*) also has noted calcareous sediments on the side of a "salt" dome on Southwest Pass. The distribution of sediments and the topographic relations, however, suggest bioherms or calcareous reefs described by Cummings and Shrock (*1*) from the Silurian of Indiana and Wisconsin. The hills perhaps may be erosional remnants, but, if so, either they must have been eroded prior to the deposition of the sandy silt forming the present continental platform or the hills protruded far enough above the surrounding flat, muddy plain to afford a place where calcareous organisms could live. The hills also conceivably could be associated with diastrophic deformation of the Gulf of Mexico basin.

The conditions of sedimentation obviously have changed profoundly in relatively recent geologic time. The upper zone of globigerina ooze, rich in calcium carbonate and characterized by a warm-water fauna, points to subtropical conditions similar to those now prevailing in the Gulf. The intermediate zone of red clay or red mud, noted in a few samples, is intermediate in carbonate content and contains a transition fauna between warm and cold. The lower zone, poor in calcium carbonate, and characterized by a cold fauna and alternating bands of clay and well-sorted silt, indicates the effect of the glacial epoch. The sediments in this bottom zone in general are essentially unchanged to the bottom of the deepest core, 250 cm. beneath the surface of the sea floor. Seemingly, therefore, only one major glacial epoch is represented.

The explanation of (1) the well-sorted, fine silt bands, (2) the layers of broken Foraminifera, and (3) the false bedding at depth in the cores offers a challenge to the imagination. Obviously, the water must have been in motion at the time of the development of the cross-bedding and also, perhaps, when the Foraminifera were broken. The false bedding, owing to the small dimensions of the core, conceivably could represent ripple marks, but, even if that is true, the bottom water must have been in motion to form ripples. How, then, could one account for deep movement of water according to prevailing notions of the sea—by tidal currents, internal waves, or deep currents? Roughness of the sea floor, just as roughness of land affects wind, must interfere with the movement of deep layers of water. But was the sea floor rough at the time of deposition of the false bedding? Perhaps the explanation lies (1) in lowering of the sea level because of removal of water during the ice age, (2) in submarine slumping, or (3) in recent deformation of the floor of the Gulf. The presence of the numerous well-sorted silt layers 200–300 miles from the present shore poses a real problem of transport. It is possible that these layers resulted from eolian action in the final stages of the ice epoch, when so much loess was being deposited. They also might have been laid down near shore. If so, our ideas of the magnitude of ocean changes in the late Pleistocene are likely to be materially different from those we have held in the past.

References

1. Cummings, E. R., and Shrock, R. R. *The geology of the Silurian rocks of northern Indiana.* (Publ. 75.) Indianapolis: Department of Conservation, 1928; Shrock, R. R. *Bull. geol. Soc. Amer.*, 1939, **50**, 529–562.
2. Shepard, F. P. *Bull. geol. Soc. Amer.*, 1937, **48**, 1349–1362.
3. Trowbridge, A. C. *Amer. Ass. Petrol. Geol.*, 1930, **14**, 867.

Obituary

Charles Atwood Kofoid
1865–1947

In the span of his life from October 11, 1865, to May 30, 1947, Charles A. Kofoid made contributions of outstanding and enduring value to biology and education. His scholarly enthusiasm left on a large number of younger biologists an impression that will influence them throughout their lives. He was an eager student of nature, a wise counselor and friend of a large number of undergraduate and graduate students, and a collector of books who had a real love for his acquisitions. He was an industrious investigator and reader and was the author of more than 200 original publications as well as several thousand reviews and abstracts. He was associated with the editing of many journals. Few who have devoted themselves to careers of creative activity and influence have been able to accomplish more than he did.

Kofoid was born at Granville, Illinois. After his courses at Oberlin were completed in 1890, he went to Harvard for graduate work. His Ph.D. thesis, completed in 1894, was a study of the early development of *Limax*, in which E. L. Mark had guided him.

The first position Kofoid had in biology was at the University of Michigan. While there, he became interested in protozoa through association with H. S. Jennings. In 1895 he was appointed to the staff of the Illinois State Laboratory of Natural History as superintendent of the Illinois Biological Station. His studies of the plankton of the Illinois River were continued for five years. In 1900 he became a member of the Department of Zoology at the University of California; and from 1910 until his retirement in 1936, except for a period of four years, he was chairman of that Department.

After Kofoid went to California, the interest in plankton that he had developed in Illinois was transferred to the ocean. In carrying on that research he took an active part in the development of the Marine Biological Station of San Diego, now the Scripps Institution of Oceanography. His investigations of plankton organisms, which were collected there and when he was naturalist on the Alexander Agassiz expedition to the eastern tropical Pacific were reported in numerous papers and ultimately in several large monographs on tintinnids and dinoflagellates. He also made some studies of dinoflagellates at the Naples Zoological Station and, when serving as Rockefeller Foundation visiting professor to Tôhoku Imperial University, at the Asamushi Biological Station in Japan.

At the time of Kofoid's trip to Ceylon in 1915 and 1916 he had become interested in intestinal protozoa and parasitology in general. He brought back ciliates from cattle and elephants, and ultimately monographic reports were prepared on them. In World War I he was commissioned major in the Sanitary Corps, engaged in a hookworm survey in Texas, and was in charge of an Army parasitological laboratory in New York City. After his return to Berkeley, he entered upon a period of intensive parasitological research. He served at one time as director of the Parasitological Division in the California State Board of Health; he conducted a laboratory making systematic examinations of persons for intestinal parasites; and he was responsible for the publication of a long series of papers on flagellates, amoebae, and ciliates of man and other animals, including termites. He was deeply concerned about public health matters, and at the end of 1921 was much interested in the possibility of going to India to occupy the chair of protozoology at the proposed Bombay School of Tropical Medicine.

Kofoid took a leading part in various undertakings in which he was able to contribute directly to public interest and welfare. At the time of his first trip to Europe he prepared an extensive report on biological stations at the request of the U. S. Bureau of Education. When he went to Ceylon and Japan, he investigated pearl culture for the U. S. Bureau of Fisheries. For many years he examined plankton from reservoirs of the San Francisco water supply, to detect and control organisms that cause tastes and odors. He directed biological studies in two cooperative projects concerning damage to wooden structures: one, that done by marine borers in San Francisco Bay and elsewhere, the other, that done by termites on the Pacific Coast. He also cooperated with the dental profession in the study of protozoa of the human mouth.

A few months before his death Kofoid turned over to the University of California his large library, accumulated jointly by himself and his wife. The collection includes 44,130 volumes not previously in the University Library. Among the books are 11,400 rare volumes in the history of science and medicine, and a complete set of all the editions of Darwin's works. His collection of reprints, which is especially complete in the subjects of protozoology and parasitology, numbers approximately 70,000.

Kofoid's professional achievements and personal distinction were recognized by election to many honorary scientific societies, including the National Academy of Sciences; by election to fellowship and to office in various organizations; by the award of diplomas and medals; by

the granting of honorary degrees by Oberlin, the University of Wales, and the University of California; and by innumerable personal and individual expressions of regard from colleagues and associates. At the time of his retirement he was given a volume of letters and manuscripts expressing appreciation from the many students who had taken the doctorate with him. A volume of the *University of California Publications in Zoology*, of which he had been an editor for 25 years, was dedicated to him. On his 80th birthday the Department of Zoology held in his honor a social meeting in his library, which occupied one of the stacks of the Biology Library in the Life Sciences Building.

Kofoid had accumulated an estate of some size. Almost all of this was left, approximately equally divided, to the University of California and the Pacific School of Religion. He intended that the gift to the University should be used to provide scholarships for graduate students, preference being given to married students. By this fund and the gift of his library he established in the University where he had spent most of his life a continuing influence of his devotion to scholarly and creative activity.

HAROLD KIRBY

University of California, Berkeley

Association Affairs

Historical Sketch of the Association

The American Association for the Advancement of Science was organized in 1848. It is the oldest general, national scientific society on this continent. For almost a century it has kept faith with its founders and has fulfilled with ever-increasing success the high purposes for which it was established.

In 1848, when the Association was organized, science consisted of two general divisions, *natural philosophy* and *natural history*, the former including the physical sciences then existing, and the latter the biological. In fact, the Association succeeded a society organized in accordance with this division of the sciences, viz., the Association of American Geologists and Naturalists, which was the culmination, in 1842, of several abortive attempts to establish a national scientific society.

The Association now has 15 sections and 202 affiliated and associated societies that together cover practically all the various fields of pure and applied science. True to the spirit that inspired its organization, the Association has continued to be an integrating factor in this growing diversity. It is a federation of various scientific organizations and disciplines which, in the long run, will prove to be among the most important forces affecting our civilization. It is demonstrating that the whole of science is greater than the sum of its parts. Perhaps the Association is rendering its greatest service to science, and to mankind in general, by providing opportunities for its professional members to consider their special subjects in the general setting of science as a whole, and to reflect on its effects upon the problems of this world.

The history of the Association shows a steadily increasing membership during the trying periods of both world wars. Even the disruptions of the greatest war in the history of mankind have not retarded its growth or impaired its vitality. The Association now has more than 33,000 members, and the membership of its affiliated societies (including duplications) is probably a million. Membership in the Association is open not only to professional scientists but also to other persons who find in science pleasure, adventure, and opportunities for service to humanity. Professional scientists have joined the Association because of the broad scope of its scientific interests, because of its journals and other publications, and perhaps even more because of the opportunities it offers for coordinating and integrating the natural sciences with social progress. Other persons have joined the Association in order to maintain contact with the great scientific currents that are sweeping humanity onward.

The annual meetings of the Association are the largest general meetings of scientists in the world. On no other occasion do men having such varied scientific interests assemble to discuss their specialties and to learn how much they have in common. With few exceptions during the period of the Civil War and World War II, the AAAS has held at least one meeting in each of its 99 years, the present one in Chicago being the 114th. The Pacific and Southwestern Divisions have held 50 meetings.

In addition to conducting meetings and conferences of those interested in the various branches of science and education, the Association edits and publishes two journals, publishes and distributes technical symposium volumes, administers gifts and bequests, provides support for research, arranges awards for scientific achievements, cooperates with other organizations for the advancement of science, and engages in other activities authorized by the Council.

The Council consists of the President, the vice-presidents of the sections, the Administrative Secretary, the General Secretary, the secretaries of the sections, the Treasurer, the members of the Executive Committee, a fellow elected by each of the two regional divisions of the Association, two fellows named by each affiliated society having more than 100 members who are fellows of the Association, one fellow named by each of the other affiliated societies, and one fellow from each affiliated academy of science. There are members of the Council representing every major field of science and interest of the Association.

A large majority of members of the Council are elected by the sections and the affiliated societies, which are entirely independent of the Executive Committee and the general officers of the Association.

It would be difficult to lodge the power of a national organization in a more representative and democratically elected body than the AAAS Council.

Not only are members of the Council democratically elected, but they represent all the special fields of science of the 115 societies which appoint them. The Council has fulfilled its obligation to speak on behalf of scientists on many occasions, most recently on legislation affecting a proposed National Science Foundation.

As the products of scientific minds exert more influence in world affairs, the responsibilities of the Association increase. With firm purpose it is serving to facilitate cooperation among scientists, improve the effectiveness of science in the promotion of human welfare, and increase public understanding and appreciation of the importance and promise of the methods of science in human progress.

[This sketch will appear in the General Program for the Chicago Meeting.]

NEWS *and Notes*

The First International Salon, "Photography in Science," sponsored by *The Scientific Monthly* and the Smithsonian Institution, is under way. For judging on October 27 competitors from 30 states and three foreign countries submitted 361 prints—243 in the black-and-white division and 118 in the color division. Most of them are being shown during November in the northwest gallery of the Arts and Industries Building, Smithsonian Institution. They will be shown again at the International Science exhibition, Chicago meeting of the AAAS, December 26 through 31. Later they may be seen at the Buhl Planetarium, Pittsburgh, and at the Cranbrook Institute of Science, Bloomfield Hills, Michigan.

The prints exhibited show novel application of photography in physical and biological research and excellent examples of photography for conventional scientific purposes. In the color division first place was awarded to Thomas C. Poulter, Armour Research Foundation; second, to Albert M. Stover, Glenn L. Martin Company; third, to Ralph O. Marts, Forest Products Laboratory. In the black-and-white division first place went to Edwin R. Willis, The Ohio State University; second, to V. P. Hollis, University of Minnesota; third, to H. U. Rhoads, Lambert Pharmacal Company.

Five entries were awarded honorable mention in each division: color—Jane K. Glaser, Argonne National Laboratory; Inez V. deGruy, Southern Regional Research Laboratory (two entries); Alice Elizabeth Sutherland, Callaway Mills; Bradford B. Underhill, Pennsylvania State College; black-and-white—Frank H. J. Figge, University of Maryland, and Thomas Carver, Harvard University, collaborating at Woods Hole; H. Lou Gibson, Eastman Kodak Company; F. A. Hamm, General Aniline & Film Corporation; Cornelius B. Philips and N. J. Kramis, Rocky Mountain Laboratory; Robert Schrek, Veterans Administration Hospital, Hines, Illinois.

Under the same auspices and title the Second International Salon will be held in Washington, D. C., in September 1948, in connection with the Centennial Meeting of the AAAS, September 13 through 18.

About People

Paul M. Gross, head, Department of Chemistry, and chairman, Research Council, Duke University, has been appointed dean of the Graduate School, succeeding **Calvin B. Hoover,** who will continue as chairman, Department of Economics.

Charles H. Philpott, principal, Harris Teachers College, St. Louis, Missouri, has been appointed director of education in charge of curriculum research and development, St. Louis Public Schools.

Carl F. Cori and his wife, **Gerty T. Cori,** both professors of biochemistry, Washington University School of Medicine, and co-winners of the 1947 Nobel Prize in Medicine, will present the third Harrison Howe Lecture sponsored by the Rochester Section, American Chemical Society, in the Rochester Chamber of Commerce building, November 17, on the topic, "The Mechanism of Enzymatic Synthesis of Polysaccharides."

James A. Baker, associate, Department of Animal and Plant Pathology, The Rockefeller Institute for Medical Research, has been appointed professor, Department of Pathology and Bacteriology, New York State Veterinary College.

John S. Nicholas, Sterling professor of biology, and chairman, Department of Zoology, Yale University, has been appointed director of the Osborn Zoological Laboratory, succeeding **L. L. Woodruff,** who died last June.

Otto A. Bessey, chief, Division of Nutrition and Physiology, Public Health Research Institute, New York City, has been appointed professor of biochemistry, and head, Department of Biochemistry, University of Illinois. He will assume his new duties on March 1, 1948.

Robert V. Drexler has been named Bert Heald Bailey professor of biology, and head, Division of Biology, Coe College, Cedar Rapids, Iowa.

Paul Kiernan, head, Section in General Surgery, Mayo Clinic, has been appointed associate professor of surgery, Georgetown University School of Medicine, Washington, D. C.

Daniel M. Popper, formerly of the staff of the Yerkes and McDonald Observatories, Universities of Chicago and Texas, has been appointed assistant professor of astronomy, University of California, Los Angeles.

J. Robert Oppenheimer, director, The Institute for Advanced Study, Princeton, New Jersey, will deliver the 1947 Arthur Dehon Little Memorial Lecture on the topic, "Physics in the Contemporary World," in Morss Hall, Walker Memorial, Massachusetts Institute of Technology, at 8:30 P.M., November 25.

e Lectureship, established in 1944 with ds donated by Arthur D. Little, Inc., memory of its founder, was inaugurated t year by Sir Edward V. Appleton, who oke on "Science, Government, and dustry."

Haven Emerson, emeritus professor public health practice, Columbia niversity School of Public Health, will liver the Cutter Lecture on Preventive edicine in Amphitheatre D, Harvard edical School, November 24 at 5:00 M. Dr. Emerson will speak on the topic, Whither the Pegasus of Public Health?"

Andrew C. Ivy, vice-president in arge of the Chicago Professional Colges, delivered the annual lecture of the psilon Chapter, Alpha Kappa Kappa, ven in memory of George A. Ulrich, inical professor of obstetrics, Jefferson edical College of Philadelphia, at the ollege on October 20. Dr. Ivy's subject as "Experiments in Resuscitation From sphyxia."

Visitors to U. S.

S. C. Pan, a member of the faculty of National Chungking University, Chungking, China, who has been appointed a Seagram International Fellow, will soon ome to this country as a visiting profesor in the Joseph E. Seagram & Sons proram.

Cenek Adamec and Ivan Viden, taff members of the Czechoslovak Institute of Public Opinion, are in this country under a grant from the Rockefeller Foundation to study various aspects of poll interviewing. Their itinerary includes the American Institute of Public Opinion, where they have been working with George Gallup, the Statistical Laboratory at Iowa State College, the University of Michigan, Harvard University, and Columbia University.

Grants and Awards

Charles R. Hook, president, American Rolling Mill Company, Middletown, Ohio, has received the 1947 Medal for the Advancement of Research from the American Society for Metals. The medal, first awarded in 1943 to Roy A. Hunt, president, Aluminum Company of America, has been won in succeeding years by Robert C. Stanley, president, International Nickel Company; Gerard Swope, General Electric Company; and Rufus E. Zimmerman, vice-president, U. S. Steel Corporation of Delaware. The medal, plaque, and citation were awarded at the annual banquet of the Society held in Chicago October 23, during the National Metal Congress and Exposition.

The American Society of European Chemists and Pharmacists, an association of scientists who have been graduated from European universities, at a meeting held in New York on November 5 presented to **Carl Neuberg,** research professor of chemistry at New York University, the newly established Carl Neuberg Medal for scientific achievement. Dr. Neuberg, who was born in Germany in 1877, is author of almost 1,000 publications and founder of *Biochemische Zeitschrift,* of which he was editor from 1906 until 1936. He was at one time director of the Kaiser Wilhelm Instituts for Experimental Therapy and for Biochemistry.

Howard G. Swann, associate professor of physiology, University of Texas Medical Branch, has received a grant of $12,500 from the AAF Laboratories for the support of research on resuscitation.

Harlow Shapley, director, Harvard College Observatory, has been awarded the Gold Medal of the Indian Association for the Cultivation of Science. The presentation was made by S. K. Banerji, member of the Governing Board of the Association, at the 95th National Meeting of the American Meteorological Society, held jointly with the American Geophysical Union's New England Meeting, September 18, at the Institute of Geographical Exploration, Harvard University.

Smith, Kline & French Laboratories, Philadelphia, has made a grant to **Stanley C. Harris,** professor of pharmacology and physiology, Dental School, Northwestern University, to enable him to conduct research on the pharmacology of analgesia and anorexia in the Dental and Medical Schools of Northwestern. **Clement A. Finch,** Harvard Medical School, has also received a grant for the support of research to be done at the Peter Bent Brigham Hospital, Boston, under the supervision of George W. Thorn, of Harvard Medical School.

The University of Michigan has received a grant of $8,500 from Parke Davis & Company, Eli Lilly & Company, Abbott Laboratories, and the Upjohn Company to permit completion of experimental research and investigation of the synthesis of penicillin and related compounds. This research is under the direction of **Werner E. Bachmann,** professor of organic chemistry at the University.

The James F. Lincoln Arc Welding Foundation has recently announced the rules of its Annual Engineering Undergraduate Award and Scholarship Program. Resident engineering undergraduate students registered in any school, college, or university in the United States which offers a curriculum in any branch of engineering (including agricultural engineering) or architecture leading to a degree, and cadets registered in the U. S. Military, Naval, and Coast Guard Academies, are eligible to submit papers dealing with design for arc welding of parts of machines, complete machines, trusses, girders, structural parts, or their maintenance. It is not necessary that the machine, structure, or part, be actually built, but the design or method of construction must be described in the paper. Papers must be mailed by May 15, 1948. A total of 77 awards are offered, the highest being $1,000; the next highest, $500; and the third highest, $250. Four awards will be given of $150 each, 8 of $100 each, 12 of $50 each, and 50 of $25 each. The departments in the institutions in which the three highest awards are made will receive amounts of money equal, respectively, to those awards, to be used as scholarships within the departments. Further information may be obtained from the James F. Lincoln Arc Welding Foundation, Cleveland 1, Ohio.

Whittlesey House and *Science Illustrated* have announced the Second Biennial Prize Contest for books on scientific subjects written for the layman. First prize is $3,500; second prize, $1,000; third prize, $500. In addition, a $1,000 advance against royalties will be given to each of the prizewinners and also to each additional author whose project is accepted for publication. The contest opens December 1, 1947, and closes November 1, 1948. Manuscripts must be completed by November 1, 1949, and range in length from 80,000 to 150,000 words. The contestant must submit by November 1, 1948, a complete plan for the book, with 15,000 words of the manuscript, and a detailed account of the amount and kind of research he intends to do. He must also supply two typewritten recommendations, one professional and one personal, plus an autobiographical sketch of at least 250 words. All entries

must be typed in English, double-spaced, and the original typescript should be submitted to Beulah Harris, Science Editor, Whittlesey House, 330 West 42nd Street, New York 18, New York.

Judges for the contest will be: Harlow Shapley, director, Harvard College Observatory; C. C. Furnas, director, Aeronautical Laboratory, Cornell University, Buffalo, New York; Paul B. Sears, professor of botany, Oberlin College, Oberlin, Ohio; Gerald Wendt, editorial director, *Science Illustrated*; and the editors of Whittlesey House. The first contest, which closed November 1, 1946, was won by Clyde Kluckhohn, Department of Anthropology, Harvard University, for his manuscript, *Anthropology and the world today*.

In October 1945, Research Corporation, New York City, established the Frederick Gardner Cottrell Grants in Aid of Scientific Research, designed to assist in re-establishing academic research programs and teaching staffs disrupted during the war. The following year over 100 grants amounting to about $430,000 were approved from the fund of $2,500,000 set aside for this purpose. These grants, which are made to institutions on the basis of applications by individuals, have gone to about 30 states, Alaska, and the District of Columbia, more than half of the recipients being smaller colleges and universities. Since its founding in 1912 by F. G. Cottrell, the Corporation has awarded more than $2,000,000 to some 120 institutions. Application forms and additional information may be secured from the Corporation's offices, 405 Lexington Avenue, New York 17, or 225 Santa Monica Boulevard, Santa Monica, California.

Colleges and Universities

Savage Hall, new headquarters of the Cornell University School of Nutrition (see *Science* cover, October 10), was officially placed in service October 10 at impressive dedication ceremonies on the campus which reflected the School's key role in the world food crisis.

The event was characterized by Governor Thomas E. Dewey, who spoke at the ceremony, as "the brightest spot I know in a period when the high price and scarcity of food are uppermost in the minds of the people of the Nation and the world." He went on to say: "This is a most fortunate time for the completion of this first building of our great new Cornell School of Nutrition. Here is a happy union of university, farmer and state cooperation, all in one effort to improve the health of the American people."

Disclosing his views on the world food crisis, he asserted: "We need and want to do our honest share to feed hungry people overseas until they are better able to help themselves. We have at the same time a prior and a binding obligation to see that no American is poorly fed as a bitter result of thoughtlessness or badly planned generosity on our part."

"The farmers of our state and Nation have performed miracles at increasing production by nearly one-third over the prewar period. We can count on the farmers as always to do more than their share, and it is a matter of real gratification that the farm organizations of New York have taken such a vital interest in the nutrition of our people by contributing this beautiful new home of the School of Nutrition. . . . I am happy and proud to dedicate Savage Hall of the Cornell School of Nutrition to the better nutrition of the American people and to the science of using food for the advancement of the health, the vigor, and the good will of human beings everywhere."

Leonard A. Maynard, director of the School, stated that the new building provides greatly strengthened facilities for carrying out an over-all program of nutrition study. He added: "This gift by the farmers of the Northeast was a pioneer action—as much as the establishment of the School itself. So far as is known, no similar contribution to a university has ever been made. The action reflects the real interest of farmers in public service, their recognition of the importance of education and research and their appreciation of the interdependence of agriculture, nutrition, and health."

Before Savage Hall was built, the School had no buildings of its own. One of its laboratories was over a horse barn and the rest of its facilities were scattered in other University buildings. Now these facilities are centralized in a four-story, brick and limestone structure with 22,700 square feet of floor space and a number of fully-equipped research and student laboratories.

The School continues, however, to draw its staff and information from the Colleges of Arts and Sciences, Engineering, Agriculture, Home Economics, the University Clinic, the College of V erinary Medicine, and the U. S. P Soil, and Nutrition Laboratory, al which contribute to an across-the-b study of nutrition that covers every p of the broad field from the soil to consumer's table.

In addition to Governor Dewey principal speakers included W. H. Se of the National Institute of Health, Congressman Clifford R. Hope, Kansas, chairman of the House C mittee on Agriculture.

Presiding at the ceremony was Ar S. Adams, provost of the Univers The building was presented to the U versity by Frank M. Smith, chairm New York State Conference Board Farm Organizations, and was accepted Neal Dow Becker, chairman of its Bo of Trustees.

At the request of the farm organi tions which contributed to the buildin was named by the Board of Trustees honor of the late Elmer S. Savage, fessor of animal husbandry in the Col of Agriculture. Prof. Savage had b associated with Cornell for 35 years, a in that time became one of the dai industry's outstanding leaders. Most his work was done in the field of dai cattle nutrition, from which came t Cornell Calf Starter Method. One of h greatest contributions was the initiati of the widely adopted "open formul plan for the marketing of livestock fee

The Medical College of Virgin was presented a portrait of Wortley Rudd, former dean, School of Pharma of the College, by the Richmond Ret Druggists Association, November 7, the Richmond Academy of Medici Dr. Rudd retired July 1 after serving years as dean and 43 years as a facult member of the College. The portrait w painted by John D. Slavin of Richmon

The University of Wisconsin h obtained a reconverted aircraft turbo supercharger of the type used to "boos bombers to heights of some 40,000 fe during the war for use in a research pro gram designed to develop new and bett fuels and superchargers for combusti engines. The program, which is bein supported by the Wisconsin Alumni Re search Foundation, will be under th direction of **Phil Myers** and **Otto Ury hara,** of the engineering faculty. Th temperatures resulting from the combus tion which powers the rotor to 22,00

p.m. will be studied by the use of n electro-optical pyrometer, which the wo men invented several years ago to tudy combustion in diesel engines. This nstrument works on the principle of the electric eye" by gauging the temperature f the rotor, or of the exploding vapor in he cylinder in the case of the diesel, by easuring the intensity of light through quartz window.

The University of Georgia, Athens, as announced the following additions to s Department of Biology: **I. C. Kitchin,** formerly associate professor of oology, University of North Carolina, ssociate professor; **Donald C. Scott,** niversity of Indiana, instructor; and **Charles O. Hathaway,** University of irginia, instructor.

At the Indiana University Medical School, Indianapolis, **Randall Thompson,** formerly of the Medical College of Virginia, has been appointed chairman of newly-created Department of Microbiology, and **Thurman B. Rice,** formerly hairman, Department of Bacteriology nd Public Health, has been named hairman of the now separate Department of Public Health.

Fellowships

Kenyon Thomas Payne, graduate student, Division of Agronomy and Plant Breeding, College of Agriculture, University of Minnesota, has been appointed Conway MacMillan Memorial Research Fellow in Botany for the academic year 1947-48. This fellowship was established at the University in 1946 by Charles J. Brand, economic consultant and alumnus of Minnesota.

The Mellon Institute of Industrial Research has announced the establishment there of a research fellowship by the Fanny Farmer Candy Shops. This fellowship, headed by **M. G. Mayberry,** will carry on wide investigations relating to important basic problems in confectionery technology. The program embraces all phases of candy ma'ing, including scientific methods for the betterment of manufacturing procedures and especially for defining and controlling the texture of products.

The Life Insurance Medical Research Fund will receive applications up to January 15, 1948, for grants in aid of research on cardiovascular problems to begin in 1948. Support is available for physiological, biochemical, and pathological research which bears on cardiovascular problems, as well as for clinical investigation in this field. About $500,000 will be awarded for these grants.

Postgraduate fellowships for training in research for 1948–49 are also available, and applications will be received for these up to January 1, 1948. Preference will be given to candidates wishing to work in the broad field of cardiovascular function or disease and to those wishing to work in institutions other than the ones where they obtained most of their experience. A Ph.D. or M.D. or the equivalent is required. About 12 fellowships will be available with annual stipends of $2,500–$3,500.

Later in the year, the Fund will also offer a number of predoctoral research fellowships. Further information may be obtained from the Scientific Director, Life Insurance Medical Research Fund, 2 East 103rd Street, New York 29, New York.

Lehigh University has recently awarded 10 graduate study fellowships, four of which went to foreign students. Among the recipients are: **Frederick R. Gardner,** Queens University, Toronto, awarded the Sinclair Printing Ink Research fellowship in chemistry; **Ching-Huan Yang,** National Central University, Nanking, China, the Lawrence Calvin Brink fellowship in civil engineering; **Bernt Roald,** Technical University of Norway, Trondheim, the Roy R. Hornor research fellowship in metallurgy; **Walter E. Munz,** Swiss Institute of Technology, Zurich, the C. Kemble Baldwin research fellowship in mechanical engineering; **Helmut Tielsch,** Alabama Polytechnic Institute and University of Michigan, the New Jersey Zinc Company fellowship in metallurgy; **Charles F. Bild,** University of Virginia, and **Donald E. Knulk,** Ohio State University, the William C. Gotshall scholarships in metallurgical engineering; **Ludwig R. Kowalski,** Duke University, the Westinghouse fellowship in mechanical engineering; and **Richard C. Huyett,** Lehigh University, the Consolidated-Vultee Aircraft Corporation fellowship in mechanical engineering.

Paul A. Geary, research chemist, Smith, Kline & French Laboratories, Philadelphia, has been awarded the second Walter G. Karr fellowship to finance his postgraduate studies in physical chemistry at the University of Pennsylvania. This fellowship was established in 1946 for scientific personnel of Smith, Kline & French Laboratories who desire to continue their academic studies.

Meetings

The 1947–48 series of Laity Lectures, given by the New York Academy of Medicine, 2 East 103rd Street, New York, began October 30 with a lecture on "The Atom in Civil Life" by Lewis L. Strauss, member of the U. S. Atomic Energy Commission and the Naval Research Advisory Board. Succeeding lectures will include: "The Psychology of Leadership in War and Peace," George Ronald Hargreaves, formerly assistant director, Army Psychiatric Division, War Office, Great Britain, November 19; "Food and Civilization," Sir Raphael Cilento, director, Division of Social Activities, United Nations, December 17; "On Being Old Too Young," Edward J. Stieglitz, chief of medical staff, Suburban Hospital, Washington, D. C., January 22; "Perspectives in Cancer Research," Cornelius P. Rhoads, director, Memorial Hospital, New York, February 4; "Psychiatry for Everyday Needs," William C. Menninger, The Menninger Foundation, Topeka, Kansas, February 26; and "The Interrelation of Pure and Applied Science in the Field of Medicine," James B. Conant, president, Harvard University, March 11. All lectures, which begin at 8:30 P.M., are free of charge and open to the public.

The American Mathematical Society will hold its 429th meeting at Washington University, St. Louis, Missouri, November 28–29. Sessions will begin at 10:00 A.M. Friday and will continue through Saturday morning. Marshall Hall, Ohio State University, will speak Friday morning on the topic, "Foundations of Geometry, Retrospect and Prospect." At 9:00 A.M. Saturday, Szolem Mandelbrojt, Collège de France and Rice Institute, will speak on "Analytic Continuation and Infinitely Differentiable Functions, a General Principle." A dinner will be held Friday at 6:30 P.M. in the McMillan Hall dining room.

The American Society of Mechanical Engineers will meet December 1–5 in Atlantic City, New Jersey, with headquarters at Chalfonte-Haddon Hall. Among the ASME guests will be David Lilienthal, who will speak at a nuclear

energy luncheon on December 2; Fred S. McConnell, president of the National Coal Association, who will address a fuels dinner Tuesday evening on "The Coal Industry Looks Ahead"; and E. O. Shreve, president of the U. S. Chamber of Commerce, who will participate in an education session on the afternoon of December 1.

In addition to nuclear energy, a second featured topic will be rocket research. In several sessions co-sponsored with the American Rocket Society, an affiliate of the ASME, the topic will be discussed by Clark B. Millikan, director of the Guggenheim Aeronautical Laboratory, California Institute of Technology, giving special attention to a review of the 10 years of research at the Laboratory, and Werner von Braun, technical director of Germany's Peenemunde Rocket Research Base during the war, who will speak on the development of the V-2 missile. A trip has been arranged to the Atlantic City Naval Air Station for demonstrations of rocket-assisted take-off, flights of A.S.F. and naval jet-propelled aircraft, and static firing of a liquid fuel rocket engine. Exhibitions of equipment and material in the fields of jet propulsion, gas turbines, and nuclear energy have been invited from the war, navy, air, engineering, and scientific branches of the Government and industry.

Sessions have also been scheduled on machine design, metals engineering, railroads, fuels, safety, process industries, power test codes, rubber and plastics, wood industries, petroleum, aviation, power, oil and gas power, hydraulics, and industrial instruments and regulators.

The American Academy of Pediatrics will hold its annual meeting December 9, in Dallas, Texas. The program will be devoted to three papers outlining the findings to date of the Academy's two-year Study of Child Health Services in Alabama, Illinois, Montana, New Hampshire, New Mexico, North Carolina, Oregon, District of Columbia, and Maryland. Warren R. Sisson, chairman, Committee for the Study of Child Health Services, will discuss "the total volume of medical care to children, based on an analysis of eight selected states." John P. Hubbard, director of the Study, will present a paper on "a review of private practice: pediatricians and general practitioners." "Facts and figures on pediatric education" will be presented by John McK. Mitchell, who has conducted the study of pediatric education through personal visits to all approved medical schools in the United States and two in Canada.

A Symposium on Northern Arizona Geology was held at the Museum of Northern Arizona, Flagstaff, on August 26. Participants were 7 graduate students in geology who spent the summer in northern Arizona working under the supervision of Edwin D. McKee, assistant director of the Museum.

The program included: "Geology of the North End of the Verde Valley," Richard Mahard, of the faculty of Dennison University, now studying at Columbia; "Upper Jurassic Stratigraphy of Black Mesa," John Harshberger, University of Arizona; "Ecology of a Permian Fauna at Walnut Canyon and Bottomless Pits," Halka Pattison, Stanford University; "Fauna and Stratigraphy of the Fort Apache Limestone," Stephen Winters, Columbia University; "Geology of Oak Creek Canyon," Brainerd Mears, Columbia University; "The Rim Rocks of Sycamore Canyon," William Price, University of Arizona; and "A Study of Pediments and Drainage Divides at Echo Cliffs," William Eames, Columbia University.

The New England Intercollegiate Field Geologists held their annual field meeting with 91 geologists participating, October 18–19 in Rhode Island, with Alonzo Quinn, chairman, Department of Geology, Brown University, as host, assisted by J. P. Schafer. A bed rock trip in the area north of Providence studied areas of the supposedly pre-Cambrian (?) Blackstone series, older plutonic rocks, Quincu granite and granite porphyry, and Wamsutta sandstone and conglomerate of Pennsylvanian age. The following day bed rock exposures in the Purgatory-Newport area, south of Providence, were studied. Glacial and shoreline features were studied by geologists led by Mr. Schafer in Exeter, along Narragansett Bay, and in the Wakefield-Watch Hill morainal area. The 1948 trip will be held in Vermont with Charles G. Doll, University of Vermont, as leader, and the 1949 trip will be conducted by Joseph Trefethen, University of Maine, at Orono.

The 50th anniversary of the founding of the Columbus Section, American Chemical Society, was commemorated at the Ohio State University on October 24 by a program on various phases of modern chemistry. Speakers included Charles Heidelberger, University of California, Berkeley; H. O. J. Fischer, Banting Institute, University of Toronto; Norman Hilberry, Argonne National Laboratory, Chicago; and Martin Summerfield, Jet Propulsion Laboratory, California Institute of Technology. Charles Allen Thomas, vice-president, Monsanto Chemical Company, St. Louis, and president-elect, American Chemical Society, delivered the address at the Fifty-Year Dinner, at which time the three remaining charter members of the Columbus Section were honored. The charter members are William McPherson, emeritus president, Ohio State University, and William Lloyd Evans and Charles W. Foulk, both emeritus professors of chemistry at Ohio State.

The International Union of Biological Sciences, financially supported by UNESCO, sponsored a symposium on the "Role of Trace Elements in Plant Physiology" at Rothamsted, Harpenden, England, November 5–6. Research workers from Australia, Denmark, Finland, France, Great Britain, Netherlands, Norway, Sweden, Switzerland, and the United States participated. A report of the symposium will be published by the Union.

NRC News

The National Research Council has announced that the Merck Fellowships, supported by Merck and Company and administered by the Council, are available for the academic year 1948–1949. This program, designed to stimulate interest in fields of study requiring knowledge of more than one science, offers fellowships to provide special training to young men and women who have demonstrated marked ability in research in chemical or biological science and who wish to broaden their fields of investigational activity. Candidates must submit evidence of training in these fields equivalent to that represented by the Ph.D. degree and must have demonstrated unusual research ability. Study abroad may be approved in some cases. The annual stipends are $2,500–$5,000, and an annual allowance of $500 is provided to the institution to which each Fellow is assigned. Fields of study will be in chemistry and biology, including the preclinical medical sciences. Initial appointments will be for a term of one year,

renewable for a second year, and, in exceptional cases, for a third year. Further information may be obtained from the National Research Council Fellowship Office, 2101 Constitution Avenue, N. W., Washington 25, D. C.

Deaths

Sister Mary Rose (Murray), professor of chemistry, College of St. Elizabeth, Convent Station, New Jersey, died of a heart attack on June 11.

Sister M. Augustina (Brobston), 81, chairman, Department of Chemistry, College of St. Elizabeth, Convent Station, New Jersey, died suddenly July 21. She had been associated with the Department since 1906.

Mary Jones Fisher, at one time associate editor of *Biological Abstracts*, and more recently affiliated with the Academy of Natural Sciences in Philadelphia, died on October 9 in Dover, Delaware.

Frederic Ewald Sondern, 80, retired clinical pathologist and formerly president, New York State Medical Society, died October 10 at Post-Graduate Hospital, New York City, after a 6-week illness.

Robert H. Lombard, 59, who for the past 20 years had been research chemist in the Norton Company Research Laboratories, Worcester, Massachusetts, where he made important contributions to the abrasive industry, died on October 11.

Frank R. Lillie, 77, Andrew MacLeish distinguished service professor of embryology emeritus, and for over 20 years chairman, Department of Zoology, University of Chicago, died November 5 in Chicago.

With the hungry of Europe looking to America for food, clothing, and dollars to help them through the coming winter, we are again reminded of a way in which we as individuals can supplement the meager rations of these people. CARE (Cooperative for American Remittances to Europe, Inc.) food packages, each containing enough food to feed supplementary meals to a family of four for a full month, in addition to baby food, blanket, cotton, woolen, knitting wool, household linen, and layette packages, may be ordered for $10 each and will be dispatched promptly to a needy European friend. The offices of CARE are located at 50 Broad Street, New York City 4.

The Federation of American Scientists has made provision for admission of members-at-large. The chairman of the Federation, **Robert E. Marshak,** in announcing the provision, has written as follows:

"The Federation of American Scientists was formed to integrate those groups of scientists which sprang up spontaneously at the end of the war to alert the public to the implications of the development of atomic energy and to work for sound legislation and policy in this field.

"Some of the major activities of the Federation have been (1) providing accurate technical information to the public and to its leaders in order to establish a basis for intelligent social action; (2) mobilizing support for civilian control of atomic energy in this country; (3) supporting the confirmation of the present members of the Atomic Energy Commission; and (4) working for a National Science Foundation. In items (2) and (3) the Federation has been particularly effective.

"Scientists have played a prominent part in national affairs in the past two years, and they must continue to fulfill their responsibilities in the future. A few of the subjects under consideration by the membership are the need for more information on the factors involved in biological warfare; the re-establishment of the international scientific community by interchange of scholars, students, and technical information; and the general problem of secrecy in science. What part the Federation will play will be determined by its members. Important policy matters are carefully checked with the membership and decisions must be approved by a large majority.

"It is recognized that the active participation of many scientists is necessary if the Federation is to be representative and effective. At present there are 2,500 members, most of whom belong to the 19 local associations. The Federation is anxious to enlarge its membership, especially in the smaller scientific communities and places where groups have not yet been formed.

"Those who have the equivalent of a Bachelor's degree in the natural sciences, mathematics, or engineering are qualified to become members-at-large, and anyone who is interested in furthering the aims of the Federation is eligible for associate membership-at-large. Dues for members-at-large are set at $5.00 per year; for sustaining members, $10.00; and for patrons, $25.00 or over.

"Inquiries are cordially invited. They should be sent to the Federation of American Scientists, 1749 L Street, N. W., Washington 6, D. C."

The Scientific American, 102-year-old monthly magazine, has been purchased by The Sciences, Inc., which plans to convert it into a new magazine of the sciences to be edited and published by **Gerard Piel** and with **Dennis Flanagan** as managing editor. It will cover the physical, biological, and social sciences, engineering, and medicine, and will occupy a place between technical and professional journals and those reporting science in popular terms. The first issue of the new magazine will appear early in 1948, its price remaining at 50¢ per copy and $5.00 per year.

Erratum: In "Effect of Rutin on Anaphylactic and Histamine Shock" by R. J. Raiman, E. R. Later, and H. Necheles (*Science*, October 17, p. 368), the first sentence of the last paragraph should read as follows: "Another explanation for the protective effect of rutin may be that it prevents the liberation of endogenous histamine, perhaps by unknown factors other than those which decrease capillary permeability."

Make Plans for—

The American Philosophical Society, autumn general meeting, November 20–21, Philadelphia.

Tennessee Academy of Science, 57th annual meeting, November 28–29, University of Tennessee, Knoxville.

American Physical Society, November 28–29, Houston, Texas.

American Society of Animal Production, November 28–29, Chicago, Illinois.

The National Joint Committee on Fertilizer Application, annual meeting, December 15, Hotel Stevens, Chicago.

The Society of American Foresters, annual meeting, December 18–20, Minneapolis, Minnesota.

TECHNICAL PAPERS

The Nature of the Iron Compounds in Red and Yellow Sandstone[1]

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The color of sandstone usually is due to some form of iron which was probably deposited in the sandbeds from chalybeate water—for example, an aqueous solution of ferrous bicarbonate. Rayleigh (*3*) has demonstrated geologically probable conditions by which both red and yellow pigments can be formed from chalybeate water. Using these conditions, he has prepared both synthetic red and synthetic yellow sandstones. Both the red and the yellow pigments were demonstrated to be iron oxides or oxide hydrates with variable amounts of water. Rayleigh did not consider the difference in water content between the red and the yellow to be significant so far as color is concerned. The present paper deals with the identity of these pigments.

Rayleigh observed that chalybeate water standing undisturbed, exposed to the air, will simultaneously form both the red and the yellow oxide; the former develops as a skin upon the surface, whereas the latter forms a precipitate in the body of the solution. Formation of the red oxide is favored by increasing the area of air-solution interface; formation of the yellow oxide, by bringing more air into solution in the chalybeate water. By exposing sand moistened with chalybeate to air at 50°C., a red synthetic sandstone was obtained; but by exposing sand submerged in chalybeate water to air at the same temperature, a yellow synthetic sandstone was formed.

The oxidation of ferrous bicarbonate solutions has been studied previously by Albrecht (*1*), Schikorr (*4*), and Baudisch and Albrecht (*2*), all of whom agree that when undisturbed ferrous bicarbonate solutions oxidize, a crust of brown material forms on the surface while a yellow precipitate deposits in the bulk of the solution. The similarity in the manner of formation indicates beyond doubt that the brown and yellow oxides of these authors are identical or closely related to the red and yellow oxides of Rayleigh. X-ray diffraction patterns showed the brown oxide to be $\gamma Fe_2O_3 \cdot H_2O$ (lepidocrocite) and the yellow oxide to be $\alpha Fe_2O_3 \cdot H_2O$ (goethite). Normally both $\gamma Fe_2O_3 \cdot H_2O$ and $\alpha Fe_2O_3 \cdot H_2O$ are yellow (*5*); but $\gamma Fe_2O_3 \cdot H_2O$ is quite unstable, decomposing to γFe_2O_3 (maghemite-red) even at 100°C. The γFe_2O_3 so formed is itself metastable and can decompose to αFe_2O_3 (hematite-red). The color of the brown or red oxide observed by these authors is thus probably due to partial decomposition of $\gamma Fe_2O_3 \cdot H_2O$. The oxidation of ferrous bicarbonate solutions containing low concentrations of CO_2 favors the formation of $\gamma Fe_2O_3 \cdot H_2O$ in bulk rather than $\alpha Fe_2O_3 \cdot H_2O$ (*3*). This may explain why γ- rather than $\alpha Fe_2O_3 \cdot H_2O$ forms in the surface of oxidizing chalybeate water.

To check and extend these conclusions about Rayleigh's oxides, samples of both the red and the yellow oxides were made up according to his directions and studied by X-ray diffraction and the magnetic balance. Chalybeate water was prepared by bubbling CO_2 through distilled water in contact with high-purity iron shavings. The solution as used contained 0.655 gram Fe_2O_3/l. The yellow oxide was prepared by simply bubbling air through the solution and filtering and drying the precipitate. The red oxide was made by dropping the chalybeate water on a slowly rotating glass cylinder, which was dried by a hot plate. The temperature of the cylinder was kept well below 100°C. The red deposit so formed was scraped from the cylinder and used without further treatment.

X-ray diffraction patterns of the yellow oxide proved it to be mainly $\alpha Fe_2O_3 \cdot H_2O$. The magnetic susceptibility was 83×10^{-6} c.g.s. units/gram—in fair agreement with that of $\alpha Fe_2O_3 \cdot H_2O$ and $\gamma Fe_2O_3 \cdot H_2O$, both of which have susceptibilities of 42×10^{-6}. On heating the sample to 200°C. for about two hours, the susceptibility rose to $1{,}200 \times 10^{-6}$, indicating the presence of some $\gamma Fe_2O_3 \cdot H_2O$, which decomposes to ferromagnetic γFe_2O_3. X-ray diffraction patterns of the red oxide showed the presence of hematite and small amounts of γFe_2O_3. The magnetic susceptibility was $2{,}200 \times 10^{-6}$ as compared with 22×10^{-6} for hematite. The magnetism, readily demonstrated with a small permanent magnet, is undoubtedly due to γFe_2O_3.

Through the courtesy of David M. Seaman, of the Carnegie Institute, a series of sandstones were obtained for study. A specimen of red St. Peter's sandstone from Mineral Point, Wisconsin, contained 0.32 per cent iron as Fe_2O_3 and had a gross magnetic susceptibility of about 5×10^{-6}. The sand itself is almost pure quartz, as is shown by the fact that extraction with warm 1:1 HCl leaves a white product whose diamagnetic susceptibility ($X = -0.43 \times 10^{-6}$) is nearly the same as that of pure quartz ($X = -0.49 \times 10^{-6}$). The iron oxide in the sample thus must have a susceptibility of $1{,}600 \times 10^{-6}$. Such a high susceptibility could have originated only with γFe_2O_3. Since γFe_2O_3 is metastable with respect to αFe_2O_3 (paramagnetic, $X = 22 \times 10^{-6}$), this high susceptibility should be lowered on heating to 500°C. This was found to be the case; the gross susceptibility for the heated sandstone was only 0.76×10^{-6}, corresponding to an oxide susceptibility of 230×10^{-6}. Of the several other sandstones examined, all had susceptibilities far greater than could be attributed to hematite, goethite, or lepidocrocite; but unfortunately, the sandstones, after acid extraction, still had appreciable paramagnetic susceptibilities, and the results could not be so clearly interpreted as in the case of St. Peter's sandstone. The susceptibilities were measured in a field strength of 2,500 gauss.

References

1. ALBRECHT, W. H. *Ber.*, 1929, **62**, 1475.
2. BAUDISCH, O., and ALBRECHT, W. H. *J. Amer. chem. Soc.*, 1932, **54**, 943.
3. RAYLEIGH, LORD. *Proc. roy. Soc.*, 1946, **186A**, 411.
4. SCHIKORR, G. Z. *Anorg. allg. Chem.*, 1930, **191**, 332.
5. WEISER, H. B. *Inorganic colloid chemistry*. Vol. II: *The hydrous oxides and hydroxides*. New York: John Wiley, 1935. Pp. 27–44.

[1] Published by permission of the director, Bureau of Mines, U. S. Department of the Interior.

Cytochrome Oxidase[1]

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Separation and purification of the components of the cytochrome oxidase complex have literally presented an insoluble problem due to the difficulties experienced in attempting to dissolve the complex. Among the many attempts to obtain a solution of the enzyme has been that of Yamagutchi, Hiroshi and Ogura (*8*), who claimed a preparation from yeast and heart muscle that was active after filtration through a Seitz filter. Keilin (*5*) repeated the work and concluded that the enzymes were not in solution. Hogness, Altschul, and Abrams (*3*) reported a soluble preparation from yeast, but not all yeasts could be used, and the oxidase from any one source was not constant. More recently, Haas (*1*) has attempted to prepare a soluble oxidase from yeast by subjecting an insoluble complex to ultrasonic radiation. He succeeded only in reducing the size of the particle. Later he prepared a soluble component which is probably cytochrome A by incubating undiluted oxidase in boiling water for 3 minutes (*2*).

A report by Hopkins, Lutwak-Mann, and Morgan (*4*) on the use of bile salts in the preparation of succinic dehydrogenase suggested to us the use of sodium desoxycholate to dissolve the oxidase complex. By this method we have obtained a preparation which, when tested with the hydroquinone-cytochrome C system at pH 7.4, is 2.5 times as active as the Keilin and Hartree oxidase preparation. It retains its activity after centrifugation for 2 hours at 18,000 × g or after having been passed through a Seitz filter. Both preparations are clear and red-brown in color. A partial purification has been achieved by fractionating with sodium desoxycholate. The fractionated preparation is 4–6 times as active as the original Keilin and Hartree oxidase from which it is made.

TABLE 1

Sample	Total protein (mg./0.25 ml.)	15-minute oxygen consumption ($mm.^3$/0.25 ml.)	QO_2 protein
Keilin and Hartree oxidase	0.202	27	400
Buffer control		7	
4 per cent desoxycholate extract	0.200	60	1,040
2-4 per cent desoxycholate fraction	0.029	26	2,480
Desoxycholate control		8	

All extracts and fractionations with desoxycholate were made on a Keilin and Hartree (*7*) oxidase (fresh lamb heart) that had been diluted 1:1 with 0.1 M Na_2HPO_4-KH_2PO_4 buffer of pH 7.4. Cytochrome C was made by the method of Keilin and Hartree (*6*), and the hydroquinone-cytochrome C test system was similar to the one used by Haas except that buffer of pH 7.4 was used instead of pH 7.1.

Table 1 summarizes the results of our first experiments. All of the enzyme preparations were diluted 1:25 with distilled water as soon as possible after having been obtained in final form. The control for the Keilin and Hartree oxidase consisted of 0.25 ml. of 0.1 M Na_2HPO_4-KH_2PO_4 buffer of pH 7.4, that for the two desoxycholate preparations of 0.25 ml., 2 per cent sodium desoxycholate. The 4 per cent desoxycholate extract was made by adding 80 mg. of desoxycholate to 2 ml. of the Keilin and Hartree oxidase, grinding in a cold mortar at 4° for 10 minutes, and centrifuging at 18,000 × g for 1 hour. The 2–4 per cent desoxycholate fraction was prepared by adding 40 mg. of desoxycholate to 2 ml. of the Keilin and Hartree oxidase, grinding and centrifuging as above, and then adding to the precipitate 2 ml. of 4 per cent desoxycholate made up in 0.1 M Na_2HPO_4-KH_2PO_4 buffer of pH 7.4. Following a grinding in a cold mortar for 5 minutes at 4°, the suspension was centrifuged for 1 hour at 18,000 × g and the supernatant tested immediately after being diluted.

The effect of 2 inhibitors on the activity of the desoxycholate–Keilin and Hartree oxidase is shown in Table 2. The enzyme preparation was made by adding 3 per cent of desoxycholate to a Keilin and Hartree oxidase, grinding in the cold for 10 minutes, and centrifuging for 1 hour at 20,000 × g. The complete inhibition by 1×10^{-3} M NaCN and NaN_3 suggests that one of the enzymes involved is probably cytochrome oxidase.

These sodium desoxycholate preparations were unable to mediate the oxidation of d-glucose by d-glucose dehydrogenase of mammalian liver, even though the diphosphopyridine nucleotide and cytochrome C were added. This observation agrees with the work of Hopkins, Lutwak-Mann, and Morgan (*4*), who were unable to catalyze the oxidation of succinate with their preparation. These reactions will be studied spectrophotometrically in the immediate future. For the present it

TABLE 2

Sample	Final concentration of inhibitor	15-minute oxygen consumption ($mm.^3$/0.25 ml.)	QO_2 protein
3 per cent desoxycholate extract*		40	1,030
	1×10^{-3} M NaCN	2	0
	1×10^{-3} M NaN_3	6	0
Desoxycholate control		6	

* Total protein = 0.140 mg./0.25 ml. at 1:25 dilution.

appears that cytochrome oxidase should be a constituent of these sodium desoxycholate–Keilin and Hartree oxidase preparations. This conclusion is based on the inhibitory action of NaCN and NaN_3 and on the fact that the oxygen consumption is reduced by about 95 per cent in the absence of cytochrome C.

References

1. Haas, E. *J. biol. Chem.*, 1943, **148**, 481.
2. Haas, E. *J. biol. Chem.*, 1944, **152**, 695.
3. Hogness, T. R., Altschul, A. M., and Abrams, R. *In* Hogness, T. R. *Cold Spr. Harb. Sympos. quant. Biol.*, 1939, 7, 121.
4. Hopkins, G., Lutwak-Mann, C., and Morgan, E. J. *Nature, Lond.*, 1939, **143**, 556.
5. Keilin, D. *In* Hogness, T. R. *Cold Spr. Harb. Sympos. quant. Biol.*, 1939, **7**, 121.
6. Keilin, D., and Hartree, E. F. *Proc. roy. Soc. Lond.*, 1937, B122, 299.
7. Keilin, D., and Hartree, E. F. *Proc. roy. Soc. Lond.*, 1938, B125, 171.
8. Yamagutchi, S., Hiroshi, T., and Ogura, Y. *Acta Phytochimica*, 1936, **9**, 103.

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Differential Rate of Death for Large and Small Fishes Caused by Hard Cold Waves

GORDON GUNTER

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In 1930 Hildebrand and Cable (*3*) noted some indication that young marine fishes survived sudden cold spells better than larger ones. Gunter (*2*) in 1938 independently made observations indicating that young poikilothermal marine animals survived cold spells better than their elders. The question was raised again in 1941 by Gunter (*2*) in a discussion of the mortality caused on the Texas Coast by the hard cold wave of 1940.

Baughman (*1*), in a recent popular account of the damage done by the January 1947 freeze on the Texas Coast, noted the peculiar absence of small redfish, *Sciaenops ocellata* (Linnaeus), among fishes killed by the freeze, although their larger congeners were quite abundant.

TABLE 1

NUMBERS, SIZES, AND MEANS OF TWO SPECIES OF FISHES TAKEN FOLLOWING THE COLD SPELL OF JANUARY 1, 1942, IN COPANO BAY, TEXAS

Species	Condition	No.	Length range (mm.)	Arithmetic mean	Median	Mode
Anchoa mitchilli diaphana	Alive	150	22–76	37.2	34.8	34.8
	Dead	38	27–68	41.2	40.5	44.3
Menidia beryllina peninsulae	Alive	127	22–74	40.0	36.3	31.2
	Dead	10	38–55	46.6	46.8	45.5
Both species combined	Alive	277	22–76	38.9	35.6	30.8
	Dead	48	27–68	42.3	43.0	44.7

On January 1, 1942, a light cold wave struck the Texas Coast. The occurrence was described by Gunter in 1945 (*2*). Since regular observations were being made at set stations at that time, it was hoped that any differential mortality occurring between young and older fishes would be detected. However, the cold spell was light and few fishes were killed. Only in Copano Bay, where two small fishes, the bay anchovy, *Anchoa mitchilli diaphana* Hildebrand, and the Gulf silverside, *Menidia beryllina peninsulae* (Goode and Bean), were killed in small quantities, were all conditions proper for comparison. Total length frequency curves for each species were drawn, and although "they might appear to be slightly indicative of a differential effect of cold on the smaller and larger fish," due to the small numbers of the sample and the slight differences shown they were not accepted as proof and were not presented. However, since the size ranges of the two species corresponded very closely, it has been decided that there is no logical reason why the two samples should not be combined to give better exposition of the data.

The conditions under which the two fishes were caught were stated in some detail by the writer in 1945 (*2*) and will not be repeated. All fishes were measured in millimeters. Although 392 anchovies were taken, only 150 were measured. All dead anchovies and all silversides taken were measured. The numbers of specimens of each species, alive and dead, the length ranges, and means for all groups, separate and combined, are given in Table 1. Application to these data of Fisher's method (*Statistical methods for research workers*, 10th ed., p. 96) for the treatment of 2 x 2 tables was made by Frank W. Weymouth, to whom the writer is much indebted. If the distributions are divided into "large" and "small" at the size giving no "small" dead fish, the 2 x 2 tables given in Table 2 are derived. The chances of getting the numbers in the cells with the observed marginal totals are 4 and 5 in 10,000, a highly significant difference in mortality for large and small fish.

These data are taken as indicative of the fact that under natural conditions the larger specimens of certain species of fishes are killed by cold waves in proportionately greater numbers than the smaller specimens. The observations bear out unchecked general observations previously made by the writer and others and cited above.

Much more extensive observations on this subject should be made both in the field and in the laboratory. Pearse and Wharton (*4*), in connection with their life-history study of the marine turbellarian, *Stylochus inimicus* Palombi, found that young worms survived induced cold better than larger specimens. This is the only experimental work on the subject with which the writer is acquainted.

TABLE 2*

	Anchoa mitchilli diaphana		
	Small (26 mm. and less)	Large (27 mm. and more)	
Alive	31	119	150
Dead	0	38	38
	31	157	188
p = .0045			

	Menidia beryllina peninsulae		
	Small (37 mm. and less)	Large (38 mm. and more)	
Alive	70	57	127
Dead	0	10	10
	70	67	137
p = .0054			

* Dividing the distributions into "large" and "small," at the length below which there are no small dead fish, gives the 2 x 2 tables, showing a significant difference in mortality of large and small fish. See text for full explanation.

Reasons for a possible differential mortality of young and old poikilothermal animals are completely unknown, and any discussion of the point would be pure conjecture. However, this subject raises many interesting questions concerning comparative and general physiology, especially as they are concerned with the phenomena of aging.

References

1. BAUGHMAN, J. L. *Texas Game and Fish*, 1947, 5, 12, 31.
2. GUNTER, G. *Ecol. Monogr.*, 1938, 8, 313–346; *Ecology*, 1941, 22, 203–208; *Publ. Inst. marine Sci.*, 1945, 1, 1–190.
3. HILDEBRAND, S. F., and CABLE, L. E. *Bull. U. S. Bur. Fish.*, 1930, 44, 383–488.
4. PEARSE, A. S., and WHARTON, G. W. *Ecol. Monogr.*, 1938, 8, 606–655.

Hemophilia: The Mechanism of Development and Action of an Anticoagulant Found in Two Cases[1]

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In this preliminary report the nature of an anticoagulant found in the circulating blood of two hemophiliacs is presented. One of these patients (W. P.) was previously reported by Lawrence and Johnson (*1*). A second case was studied by Munro and Jones (*4*), who felt that the anticoagulant appeared as a result of repeated transfusions. Later analysis of the blood of this patient (*3, 5*) revealed the anticoagulant to be associated with the gamma globulin fraction of blood.

TABLE 1

DEMONSTRATION OF ANTICOAGULANT EFFECT OF BLOOD OF PATIENTS W. P. AND D. M. ON NORMAL BLOOD

Tube No.		1	2	3	4	5	6	7	8	9	10
Patient's blood (cc.)		0.0	0.0	0.0	0.4	0.8	1.2	1.6	2.0	2.0	2.0
Normal blood (cc.)		2.0	2.0	2.0	1.6	1.2	0.8	0.4	0.0	0.0	0.0
Clotting time (min.)											
Patient	Date										
*W. P	9/ 9/46	8	8	8	7	8	8	8	70	71	68
W. P.	4/24/47	6	6	7	8	10	16	36	60	52	60
W. P.	4/29/47	7	7	6	10	12	18	40	58	56	58
D. M.	4/22/47	8	6	6	14	15	16	17	75	73	75
D. M.	4/23/47	6	6	6	9	14	15	16	100	98	95

* This test was performed 8 months after the last transfusion.

The two cases included in this report are typical, proven hemophiliacs, each having had the disease since childhood. It had been observed that, at various periods when hemorrhage was severe, each would become refractory to treatment, continuing to bleed with elevated coagulation times in spite of repeated transfusions. At such a time an anticoagulant was found in the circulating blood of W. P. by Lawrence and Johnson (*1*). However, in the interim between hemorrhagic episodes both patients were relatively asymptomatic. During such a period W. P. was tested for the presence of an anticoagulant, and none was found.

At the time of admission to this hospital, both patients were bleeding severely, W. P. from the gastrointestinal tract and D. M. from the genitourinary tract. Each was immediately given whole fresh blood, unfortunately before an anticoagulant test was performed. However, the coagulation times were followed at ½-hour intervals. W. P. was found to show no response at all, either symptomatically or as measured by the coagulation time. D. M. responded transiently to the first transfusion, the coagulation time falling from 60 to 15 minutes, but rising again over a 3-hour period. Subsequent transfusions resulted in no improvement either clinically or by laboratory findings. In fact, in the case of D. M. it was noted that, after two transfusions of whole fresh blood and two injections of one vial each of antihemophilic globulin (Fraction I of Cohn–Squibb), the coagulation time had risen from an average of 60 minutes to 120 minutes.

Following these observations, both patients were tested for the presence of a circulating anticoagulant as follows:

After first injecting 5 cc. of saline, 10 cc. of blood were removed at exactly the same moment and rate from the patient and a normal subject, respectively. The two samples were then mixed in varying amounts in clean, graduated, 15-cc. centrifuge tubes which had been rinsed with saline. The results (Table 1) were found repeatedly and indicated definitely the presence of a circulating anticoagulant which had the ability to prolong the coagulation time of normal blood. Control tests performed with the blood of two ordinary hemophiliacs gave negative results, the clotting time being normal in all tubes in which any normal blood was present. The anticoagulant could also be demonstrated by mixing plasma from the patients with normal plasma in varying amounts.

An attempt was then made to determine which phase of coagulation was inhibited by this anticoagulant. The prothrombin concentration and conversion rate were normal for both patients, thus eliminating the presence of anti-prothrombin. Antithromboplastin, as described by Tocantins (*7*), was not present because, even though the blood was handled in such a way as to destroy the antithromboplastin which he described, the anticoagulant effect was still present. Also, tests using thromboplastin serially diluted to the point where its action on normal plasma was delayed failed to show any greater delay in prothrombin conversion when the plasma of either patient was used. Antithrombic activity was not found to be present since, when a known amount of thrombin (2 units) was added to the plasma of the patients (0.1 cc.), clotting occurred in the normal time. Antifibrinogen was not present since the final fibrin clot which formed in these cases was normal in its volume, retraction, elasticity, and strength. Therefore, it was evident that the anticoagulant was not antagonistic to any one of the components of the classical theory of coagulation.

Electrophoretic fractionation of the plasma of W. P. was performed by Eric Alling. Of the four fractions separated in this manner, one (fraction #1) contained only gamma globulin, and another (fraction #4) contained all components except gamma globulin. Each of these fractions was then tested for its anticoagulant activity. It was found that all fractions except fraction #4 inhibited the coagulation of normal plasma. Therefore, the anticoagulant was associated with gamma globulin. This finding is similar to that of Munro (*5*).

Since the anticoagulant was a gamma globulin and since it appeared only after repeated transfusions of whole blood or injections of antihemophilic globulin, it was thought conceivable that the anticoagulant might be the result of an "immunization" of the patient with some substance present in normal blood or Fraction I of Cohn but lacking in the patient's blood. Consequently, precipitin tests were performed using the sera of the two patients against serial dilutions of Fraction I of Cohn, containing a known amount of protein and adjusted to a pH of 7.0. There were positive precipitins in the sera of both patients, W. P. being positive at 1/320 and D. M. at 1/160. Control tests using normal sera, sera from nonhemophilic patients who had received frequent trans-

[1] This document is based on work performed under Contract No. W-7401-eng-49 for the Atomic Energy Project at the University of Rochester.

fusions, and sera of ordinary hemophiliacs were negative. Control antigens of purified gamma globulin, human fibrinogen, and albumin gave negative results. These titers were obtained repeatedly, no change being noted throughout the hospital stay, in spite of repeated transfusions.

The anticoagulant was then shown to inhibit directly antihemophilic globulin. Taylor, *et al.* (*6*) have shown the *in vitro* effect of antihemophilic globulin in lowering the clotting time of hemophiliac patients. This could be repeated by us in the case of ordinary hemophiliacs who responded to blood or plasma in the usual fashion. However, in the two patients presented no effect was noted. Also, if the antihemophilic globulin was first incubated with the proper amount of serum from each of these patients, its acceleratory action on the clotting time of ordinary hemophilic blood was lost. If the globulin was incubated with the same amount of normal or ordinary hemophilic serum, the activity of the globulin when added to the blood of an ordinary hemophiliac was unimpaired.

It was evident from these results that the antihemophilic globulin, which alone had such a marked acceleratory effect on ordinary hemophiliac blood, was in some way tied up by the sera of these two patients. In view of the demonstration of definite precipitins in their sera it was felt that the sera probably inhibited or tied up the antihemophilic globulin by means of an antigen-antibody reaction.

On the basis of the evidence presented the following hypothesis was formed to explain the presence of the anticoagulant in these two patients. Each was deficient in, or lacked, the substance known as antihemophilic globulin in his blood—a substance shown to be essential for the coagulation of blood in the normal time. Just where this globulin enters into the coagulation mechanism is unknown, but it would seem that it is necessary for liberation of thromboplastin from platelets in the first stage of clotting. When this globulin is given intravenously to ordinary hemophiliacs, either in the form of fresh blood or plasma or antihemophilic globulin contained in Fraction I of Cohn, it causes a marked acceleration of coagulation (*2*). In these two cases repeated injections of this globulin are thought to have resulted in the formation of antibodies against this globulin. These antibodies, of course, have the ability to inhibit any globulin which is later given. Therefore, these patients became refractory to further transfusion or injection of Fraction I. No beneficial effect resulted from further injections since the active globulin factor which was being given, and which is necessary for normal coagulation, was immediately rendered ineffective by the circulating antibodies. Likewise, the circulating antibodies would exert an anticoagulant effect when the patients' blood was mixed with normal blood *in vitro* by inhibiting the globulin substance present in normal blood.

The explanation proposed for the development of a refractory state to transfusion in these two hemophiliacs, based upon an immunologic response to injections of a globulin fraction deficient or lacking in their blood, may also be the underlying factor in the refractory phase manifested by many hemophiliacs. The appearance of specific antibodies which inhibit antihemophilic globulin, and thus delay the coagulation of normal blood, may depend upon several factors which are not yet clear. Whether or not a complete absence of this globulin from the blood of the hemophiliac receiving transfusions or injections of the globulin is mandatory for the development of these antibodies is not known. Perhaps there are varying degrees of hemophilia accompanied by varying degrees of deficiency of this globulin and varying ability to respond to injections of the globulin. In some of those who have a marked lack, or perhaps a complete absence, of the globulin in their blood the response would be "isoimmunization" with the development of antibodies against the injected globulin. These cases would show a refractory state to further injections of globulin, and their blood would demonstrate anticoagulant activity when added to normal blood.

Further investigation is to be carried on to determine if a mechanism such as that described is more generally applicable to hemophiliacs who become refractory to treatment.

References

1. Lawrence, J. S., and Johnson, J. B. *Trans. Amer. clin. clim. Ass.*, 1941, **57**, 223
2. Lewis, J. H., *et al.* *J. Hematol.*, 1946, **1**, 166.
3. Munro, F. L. *J. clin. Invest.*, 1946, **25**, 422.
4. Munro, F. L., and Jones, H. W. *Amer. J. med. Sci.*, 1943, **206**, 710.
5. Munro, F. L., and Munro, M. P. *J. clin. Invest.*, 1946, **25**, 814.
6. Taylor, F. H. L., *et al.* *J. clin. Invest.*, 1945, **24**, 698.
7. Tocantins, L. M. *Amer. J. Physiol.*, 1943, **139**, 265.

A Homogeneous Emulsion of Fat, Protein, and Glucose for Intravenous Administration

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Several investigators (*3*) have reported success in the preparation of various types of fat emulsions, some of which were well tolerated on intravenous injection into animals. Also, experimental evidence has been produced to show that such fat administered intravenously was properly metabolized for energy utilization (*2*) and was not lost in either urine or feces. Intravenous studies of emulsions combining the three primary foodstuffs were attempted only once (*1*), and, had this procedure been routinely practical, it would have constituted another advance in surgical parenteral nutrition.

Egg lecithin, soybean phosphatides, and other chemical agents have been used as stabilizers in the emulsification and homogenization of fat. Such emulsions, although well tolerated in some cases, have not been uniformly dependable for intravenous injection because of varying degrees of toxicity believed to be due to the chemical complexity of the stabilizing agent. Hydrophilic colloids, both acid and alkaline, were used in the stabilization of fat but on biological investigation were discarded because of the frequency of fatal embolism after injection of emulsions prepared in such manner.

In this laboratory two satisfactory types of fat emulsion have been prepared. The first type was an emulsion of coconut oil and serum albumin which, on homogenization, yielded a highly stabile preparation well tolerated intravenously. The

[1] The cooperation of Profs. Mulholland and Co Tui is gratefully acknowledged.

second type, derived from glucose, protein, and fat, was prepared in the manner described below from solutions which are commercially available in sterile containers and from a neutral saturated coconut oil which can easily be sterilized with safety. The following represents the basic proportions of the ingredients which are mixed in a 5-gallon, sterile flask: 1 l. of 6 per cent infusion gelatin (Knox P-20), 1 l. of protein hydrolysate 5 per cent amino acid solution, 200 cc. of 50 per cent glucose solution, and 100 grams of pure, refined, edible coconut oil.

After thorough mechanical agitation, the mixture is put through the Logeman homogenizer, an instrument so constructed as to make possible sterilization of its working parts. After this procedure of emulsification and homogenization, the material is collected in sterile vacuum bottle dispensers without any other processing and stored in the refrigerator. Refrigeration converts the emulsion into a solid gel which can be restored to the liquid state by warming the dispensing flask in hot water. Refrigerated samples have maintained complete stability after two months storage. Test samples of the pH of the emulsion averaged 6.5. The droplets were smaller in size than that of the canine erythrocyte and were comparable to that of the chylomicra. The concentrations of fat protein and glucose were approximately 5 per cent each and averaged 800 cal./l. The gelatin acted as a stabilizer, partially as a source of nutrient energy, and served to maintain colloid osmotic pressure.

This emulsion was administered intravenously to 7 dogs and 12 hospital patients. In the latter group at hourly intervals for a period of 8 hours during and after the infusion, temperatures, blood pressure readings, and blood samples were taken. In both groups there occurred no serious untoward reactions as were indicated by the latter studies. Two of the animals received 150 cc. of this emulsion (approximately 7.5 grams of fat) daily for 35 days. The others were sacrificed at varying times for evidence of fatty degenerative changes in the liver, lung, brain, and other organs. Microscopic examination of osmic acid, Sudan III, and hematoxylin eosin preparations failed to show evidence of lipoid granulomatosis. Three patients were maintained exclusively on this emulsion during the postoperative period with satisfactory results. One malnourished patient received with benefit a total of 5,500 cc. of the emulsion (approximately 200 grams of fat) intravenously for a period of 8 days. The emulsion caused no thrombosclerotic changes in the recipient vein and was nonirritating when infiltrated into tissue. Vitamin B and methyl donators were supplied to ensure utilization of fat. Penicillin could be added to the emulsion for intravenous administration.

References

1. Clark, D. E., and Brunschwig, A. *Proc. Soc. exp. Biol. Med.*, 1942, **49**, 329.
2. McKibbin, J. M., Ferry, R. M., Jr., and Stare, F. J. *J. clin. Invest.*, 1946, **25**, 679.
3. McKibbin, J. M., Pape, A. T., Ferry, R. M., Jr., and Stare, F. J. *J. lab. clin. Med.*, 1945 **30**, 488; Narat, J. K. *Amer. J. digest. Dis. Nutrition*, 1937, **4**, 107; Dunham, L. J., and Brunschwig, A. *Arch. Surg.*, 1944, **48**, 395; Holt, L. E., Jr., Tedwell, H. C., and Scott, T. F. M. *J. Pediat.*, 1935, **6**, 151.

IN THE LABORATORY

The Importance of Controlling Cooling Temperatures During Embedding in Paraffin

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Many textbooks of microtechnique (*1*) urge the use of only enough paraffin to cover the specimens and the use of cold water for solidifying paraffin in the process of embedding. Johansen recommends using ice water when embedding during hot weather. Unfortunately, our laboratory has found that this is not always sound advice. The use of cold water for solidifying our particular embedding mass had always resulted in cavitation or numerous low-density areas. Usually the cavities were quite large and were located in the central portion of the block, separated from, or adjacent to, the embedded materials. In an attempt to rectify the situation a series of experiments were carried out. In the light of Johansen's recommendation to use ice water for cooling, it should be stated that the experiments were conducted during the month of August, when temperatures in the room where embedding was done were 90–95° C.

In the first experiment an embedding mass[1] with a boiling point of 54–56° C., heated to 56° C., was poured into paper "boats" 2½ inches long and ¾ inch wide. No specimens were embedded. Some of the "boats" were filled (¾ inch thick), others were poured medium full (½ inch thick), and only a thin layer (¼ inch thick) was poured into others. The paraffin in three such sets was solidified in water at 9° C., 22° C., and 34° C., respectively. In each case the surface of the paraffin was blown upon, and as soon as a supporting crust was formed, the boat was submerged for 12 hours. At the end of the 12-hour period, the boats were dried and the paraffin blocks removed.

Upon cutting the blocks it was found that those medium full and full which had been cooled at 9° C. had large (3 mm. in diameter) continuous or discontinuous cavities throughout the central portion. Both top and bottom surfaces were decidedly concave. The corresponding blocks cooled at 22° C. and 34° C were solid and of desirable texture throughout. The top surface of both sets was concave. The bottom surface of those cooled at 34° C. was either level or slightly convex; that of those

[1] A mixture of 360 grams of Parawax 40 grams of bayberry wax, and 80 grams of stock rubber paraffin (1 pound of Parawax, 10 grams of crude rubber, and ½ gram of asphaltum).

cooled at 22° C. was concave but not as deeply so as in the case of those cooled at 9° C. The shallowly poured block cooled at 9° C. was solid and of good texture throughout. The shallowly poured blocks cooled at 22° C. and 34° C. were somewhat frothy with small cavities (less than 1 mm. in diameter) throughout the central portion from top to bottom and to within 3 or 4 mm. of each side. The bottom of the shallowly poured block cooled at 9° C. was slightly concave, at 22° C. flat, and at 34° C. slightly convex.

Solid pieces of paraffin shaped from comparable locations in blocks cooled at 9° C., 22° C., and 34° C. were sectioned at 5μ and 10μ. All pieces cut equally well and formed excellent ribbons. Pieces of each ribbon were placed on dry slides as well as on slides smeared with Haupt's adhesive and flooded with 3 per cent formalin water. The wet slides were placed on a warm plate, and after the ribbons had flattened and the water had evaporated, both sets of slides were examined microscopically at 125 and 537 magnifications. No consistent differences in texture, crystal size, or any other characteristic could be perceived or measured.

After establishing an optimum cooling temperature range (22–34° C.), large, medium, and small pieces of plant materials were embedded in boats poured full and medium full of paraffin. When these were cooled at various temperatures within the range, the same kinds of results were obtained as for the solid paraffin blocks.

It is improbable that all types of embedding masses have the same optimum cooling range. For this reason it would seem desirable, especially if unsatisfactory results have been obtained, to establish a range for cooling the particular embedding mass used. For practical purposes the complete optimum temperature range need not be determined. It may be found that very low temperatures resulting from icing the water will produce the best results in some cases. They certainly do not give acceptable results in all cases.

In order to determine the effect of disturbing the cooler bottom layer of paraffin soon after pouring, a boat was poured medium full of paraffin at 56° C., and the bulb of a glass thermometer heated to the same temperature was moved in and over the cooler layer of paraffin in a manner resembling rather rough orientation of materials. Care was taken not to introduce air into the paraffin by lifting and lowering the bulb of the thermometer above the surface. Before crystals began forming on the surface, the thermometer was removed, and the boat of paraffin was cooled within the optimum temperature range. The resulting block was solid but had scattered, minute, low-density areas throughout. This experiment was repeated using a "cold" (room temperature) dissecting needle. The resulting paraffin block contained small holes in the disturbed layer at the bottom of the block and numerous, low-density, pin-point spots throughout much of the block.

Our experiments have shown, therefore, that (*1*) for consistently good results, paper embedding boats should be well filled with paraffin to a depth of ½ inch or more; (*2*) an optimum cooling temperature range should be determined for each type of paraffin embedding mass used; (*3*) rapid cooling of some embedding masses does not appreciably improve the quality of the block to be sectioned; (*4*) the use of cold water for cooling may result in cavitation and low-density areas; (*5*) paraffin blocks with flat bottoms may be obtained by choosing the correct cooling temperature; and (*6*) material orientation maneuvers should be held to a minimum and be performed with instruments warmed to the temperature of the embedding mass.

Reference

1. Chamberlain, C. J. *Methods in plant histology.* (5th ed.) Chicago: Univ. Chicago Press, 1932; Johansen, D. A. *Plant microtechnique.* New York: McGraw-Hill, 1940; Lee, Bolles. *The microtomist's vade-mecum.* (10th ed.) Philadelphia: Blakiston, 1937; Sass, J. E. *Elements of botanical microtechnique.* New York: McGraw-Hill, 1940.

The Demonstration of Naturally-occurring Streptomycin-resistant Variants in the Human Strain of Tubercle Bacillus H-37RV[1]

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The development of resistance by tubercle bacilli to streptomycin is of considerable practical importance. To help elucidate this problem, an attempt was made to demonstrate the presence of naturally-occurring resistant variants in a stock laboratory strain of H-37RV by examining a large number of organisms. Variants highly resistant to streptomycin have been demonstrated in cultures of *Shigellae* (*5*), strains of *Staphylococcus aureus*, *Staph. albus*, *Proteus vulgaris*, and *Escherichia coli* (*4*), and *Hemophilus influenzae* (*1*).

TABLE 1

	Streptomycin (μg./cc.)				
	0.74	0.37	0.18	0.09	Control
Growth after 3 weeks	0	0	+++	++++	++++
	0	0	+++	++++	++++

TABLE 2

	Tubes with growth			% showing growth		
	3 weeks	4 weeks	Total	3 weeks	4 weeks	Total
Series I, 100 tubes	3	5	8	3	5	8
Series II, 40 tubes	2	0	2	5	0	5

Cultures were made in the liquid medium described by Dubos (*3*), using 10-cc. rather than 5-cc. quantities. A single 4-week-old culture of the human laboratory strain H-37RV growing in Dubos medium was used as the source of the test organisms. The concentration of tubercle bacilli (mg./cc.) was determined by turbidimetric readings in calibrated tubes, using a blue filter (420 mμ) in a Lumetron colorimeter. Streptomycin assays on the supernatant fluid were done, using *Klebsiella pneumoniae* #41 as the test organism according to the method described by Alture-Werber and Loewe (*2*).

Series I: Each of 100 tubes of Dubos medium containing 18.5 μg. of streptomycin/cc. was inoculated with 0.1 mg. of the test culture of H-37RV.

[1] Supported by a grant from the U. S. Public Health Service. We are indebted to William Steenken, of the Trudeau Laboratory, for the strain of H-37RV and to G. Rake, of the Squibb Institute for Medical Research, for the strain *Klebsiella pneumoniae* #41.

Series II: Each of 40 tubes containing 37 μg. of streptomycin/cc. was inoculated with 0.2 mg. of H-37. A routine streptomycin sensitivity assay was done on organisms from the same culture used to inoculate Series I and II with an inoculum of 0.1 mg. Tubes showing growth in Series I and II were centrifuged, the supernatant saved for streptomycin assay, and the bacilli resuspended in fresh Dubos medium. A turbidimetric reading was made and 0.1-mg. amounts were inoculated into tubes for a second streptomycin sensitivity assay.

The assay on H-37 done in duplicate gave 0.37 μg. of streptomycin/cc. as the amount necessary to inhibit growth completely (Table 1). These results agreed with previous testing of this particular strain done in this laboratory. It is apparent that the tubes in Series I contained 50 times the amount of streptomycin necessary to produce complete inhibition of growth, and those in Series II, 100 times the amount.

At the end of 3 weeks, 3 tubes in Series I and 2 tubes in Series II showed definite growth. At the end of 4 weeks, 5 additional tubes in Series I showed growth (see Table 2).

Streptomycin sensitivity assays were done on cultures which showed growth in Series I and II, and the results given in Fig. 1 are representative. The turbidimetric values plotted in the graphs are an average of readings of 4 tubes in each series. Note that the base line for tubes containing 3,700 μg./cc. is at 75. The high concentration of streptomycin gave a distinct yellow color to the medium and resulted in the high initial reading, since the blank tube used for all readings contained only Dubos medium.

Only a fraction of the tubes containing 50–100 times the amount of streptomycin capable of producing complete bacteriostasis on routine sensitivity assay showed growth. The bacilli which multiplied, however, showed a remarkable resistance to streptomycin, being capable of growing in 10,000 times the amount initially adequate to prevent growth. It can be seen in the graph that growth curves for tubes containing up to 1,000 times the amount of streptomycin usually inhibitory parallel the curve for the control tube. If anything, they show a more rapid growth than the controls. Tubes containing 3,700 μg. showed a flatter curve, but growth was quite distinct.

Assays done on the supernatant fluid showed 2 μg./cc. in Series I and 4 μg./cc. in Series II at the end of one month. The tubercle bacilli from these same cultures showed resistance to 3,700 μg./cc. in a subsequent sensitivity assay. Obviously, there had been a gradual loss of streptomycin activity, but even at the end of a month the amount of streptomycin present in Series II was more than 20 times that necessary to inhibit growth in the initial assay.

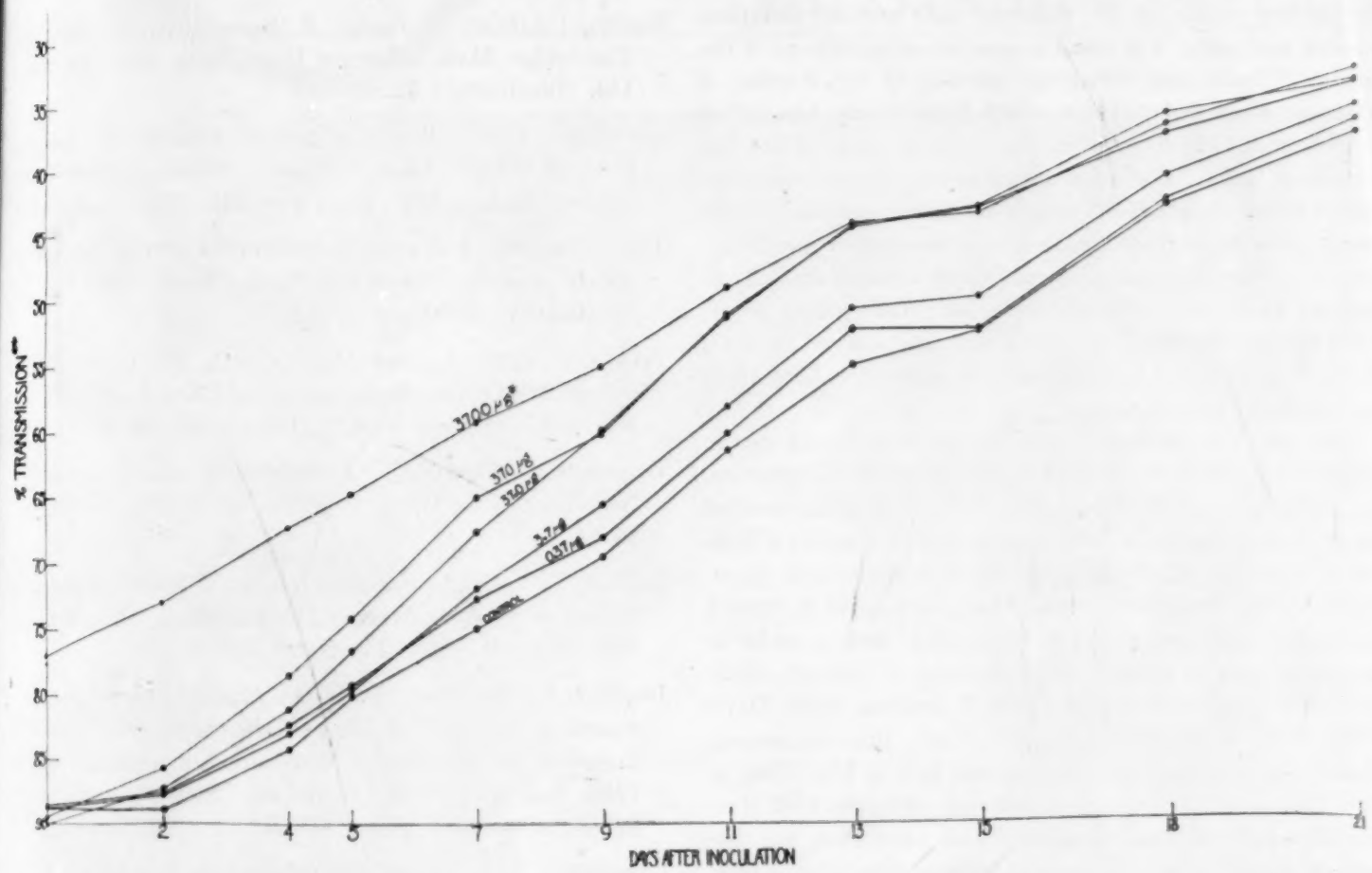

FIG. 1. Streptomycin sensitivity assay on resistant organisms from Series I: * micrograms of streptomycin/cc. of medium; ** % transmission using the blue filter (420 mμ) in a Lumetron colorimeter.

Thus, by using large numbers of bacilli it is possible to demonstrate the occurrence of streptomycin-resistant variants of tubercle bacilli in cultures not previously exposed to streptomycin. It is possible that these naturally resistant variants play a part in the development of streptomycin resistance *in vivo*.

References

1. ALEXANDER, H. E., and LEIDY, G. *J. exp. Med.*, 1947, **85**, 607.
2. ALTURE-WERBER, E., and LOEWE, L. *Proc. Soc. exp. Biol. Med.*, 1946, **63**, 277
3. DUBOS, R. J., and DAVIS, B. D. *J. exp. Med.*, 1946, **83**, 409.
4. KLEIN, M. *J. Bact.*, 1947, **53**, 463.
5. KLEIN, M., and KIMMELMAN, L. J. *J. Bact.*, 1946, **52**, 471.

Book Reviews

A history of the American Medical Association, 1847-1947. Morris Fishbein. Philadelphia-London: W. B. Saunders, 1947. Pp. xvi + 1226. (Illustrated.) $10.00.

This revealing volume is not a critical analysis of the development of the most important medical organization in the United States, but rather a chronology of its activities during its first century of existence, as abstracted from its *Transactions*. Projected in 1929, the satisfactory compilation of the book was delayed by World War II. It was pushed to publication for the centennial meeting of the AMA in May 1947 by the driving efforts of Dr. Fishbein with hurried dictation, scissors, and paste. The result is sometimes reminiscent of the famous "Tonics and Sedatives" section of the *Journal of American Medical Association*, which Dr. Fishbein has edited so well since 1924. Dr. W. L. Bierring's accounts of the 101 presidents of the Association are customary professional eulogies. Various Association officials offer short sketches of the many councils, bureaus, publications, and other special activities of the Association. From these it is clear that, in contrast to its first 50 years, the second half-century of the AMA has been extremely successful in a practical and financial sense. There are chronological data in appendixes, and there are name and subject indexes.

The American Medical Association arose a century ago in response to serious abuses in medical education and practice. The rapid expansion of the country, with the resulting need for many doctors, caused a mushroom growth of medical schools and a large output of unsatisfactory and unqualified physicians. A number of abortive attempts were made to form a national organization of competent medical men, in order to raise standards of medical education and of medical ethics. Thanks to the persistence and skill of Nathan Smith Davis (1817–1904) of Binghampton, New York, this was accomplished. An organizational meeting was held in May 1846, in New York, and the first convention with delegates took place the following year in Philadelphia. The Association has consistently maintained a democratic organization through delegates elected by State Medical Societies. After a century of intensive effort, it is clear that the prime purpose of the AMA in raising standards of medical education has been brilliantly achieved. Unfortunately, there still remains much confusion about "medical ethics." However, the majority of physicians are agreed regarding their standards of professional etiquette and general morality, and this is an important advance. There is now growing appreciation that general principles of ethical conduct are more significant than a multiplicity of detailed rules.

An outstanding public contribution of the AMA has been the gradual suppression of medical quackery. This part of the story is told with relish, and with details of libel suits brought by various quacks as a result of published AMA reports. There is also much in justification of the AMA's stand on "socialized medicine."

The official centennial story of the Association is an interesting social document for scientists. It illustrates the difficulties and disappointments inherent in the development of large professional organizations, and suggests the wisdom of frequent, honest, and good-natured self-criticism in such organizations for the promotion of professional standards and practices.

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Scientific Book Register

BOYD, WILLIAM C. *Fundamentals of immunology.* (2nd ed.) New York-London: Interscience, 1947. Pp. xvi + 503. (Illustrated.) $6.00.

BRUES, CHARLES T. *Insects & human welfare.* (Rev. ed.) Cambridge, Mass.: Harvard Univ. Press, 1947. Pp. xiii + 154. (Illustrated.) $2.50.

COPELAND, EDWIN BINGHAM. *Genera Filicum: the genera of ferns.* Waltham, Mass.: Chronica Botanica; New York: Stechert-Hafner, 1947. Pp. xiv + 247. (Illustrated.) $6.00.

DYK, WALTER. *A Navaho autobiography.* (Publ. in Anthropology, No. 8.) New York: Viking Fund, 1947. Pp. 218. (Illustrated.) $3.00.

EAMES, ARTHUR J., and MACDANIELS, LAURENCE H. *An introduction to plant anatomy.* (2nd ed.) New York: McGraw-Hill, 1947. Pp. xvii + 427. (Illustrated.) $4.50.

GLAESSNER, MARTIN F. *Principles of micropalaeontology.* New York: John Wiley, 1947. Pp. xvi + 296. (Illustrated.) $6.00.

JAGGAR, T. A. *Origin and development of craters.* (Geological Society of America, Memoir 21.) Baltimore, Md.: Waverly, 1947. Pp. xvii + 508. (Illustrated.) $6.00.

JOSEPHY, E., and RADT, F. (Eds.) *Elsevier's encyclopaedia of organic chemistry.* (Vol. 13, *Tricyclic compounds*: Series III, *Carboisocyclic compounds.*) New York-Amsterdam: Elsevier, 1946. Pp. xx + 1265. Single vol., $104.00; serial price, $91.00; subscription price, $78.00.

LASKOWITZ, I. B. *Designs for helicopters.* Brooklyn, N. Y.: I. B. Laskowitz, 284 Eastern Parkway, 1947. Pp. 23. (Illustrated.) $2.00.

MIGRDICHIAN, VARTKES. *The chemistry of organic cyanogen compounds.* (American Chemical Society Monograph Series.) New York: Reinhold, 1947. Pp. ix + 460. $12.00.

SLIJPER, E. J. *Comparative biologic-anatomical investigations on the vertebral column and spinal musculature of mammals.* Amsterdam, Holland: N. V. Noord-Hollandsche Uitgevers-Maatschappij, 1946. Pp. 128. (Illustrated.)

TOMKINS, SILVAN S. *The thematic apperception test: the theory and technique of interpretation.* New York: Grune & Stratton, 1947. Pp. xi + 297. $5.00.

WITT, J. C. *Portland cement technology.* Brooklyn, N. Y.: Chemical Publishing Co., 1947. Pp. 518. $10.00.

WOLFF, WERNER. *What is psychology: a basic survey.* New York: Grune & Stratton, 1947. Pp. xii + 410. (Illustrated.) $4.00.